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UNIVERSITY OF PENNSYLVANIA MEDICAL BULLETIN.

FURTHER OBSERVATIONS ON THE ENDEMIC OCCURRENCE OF CARCINOMA AND ON THE INOCULABILITY OF TUMORS.

By Leo Loeb, M.D.,
Assistant Professor of Experimental Pathology.

(From the Laboratory of Experimental Pathology, University of Pennsylvania.)

About seven years ago I published, with Dr. George Johson,[1] some observations on the endemic occurrence of carcinoma in cattle. We found a ranch in Wyoming in which a relatively large proportion of cases of carcinoma of the inner angle of the eye in cattle had been observed in the course of the last ten years. These observations corresponded to those made on human beings by Behla and others some time before. We left it undecided whether or not that endemic occurrence had to be explained by the presence of a micro-organism. We noted, especially, that no peculiar conditions which differed from those of the neighboring ranches, which were practically free from cancer, existed on that ranch in Wyoming.

I[2] published further observations on the endemic occurrence of cancer in rats which were affected with sarcoma. From 1900 1903 I found in a few cages which were standing side by side in the Polyclinic of Chicago, in the course of three years, three rats all of which had cystic sarcoma of the thyroid gland. The main facts may be stated as follows: In a few cages, which were kept very clean, tumors were observed among animals which received a certain regular food which usually had been boiled. All the tumors were found on the same part of the body, and showed the same macroscopic and microscopic structure. These tumors preserved, in the main, their character during the course of many transplantations. It was especially noticed that such tumors were found in animals a relatively long time after the last animal affected, with such a tumor, had been removed from the laboratory. It was further found that in other cases in which an endemic occurrence of tumors had been observed, the tumors had about the same structure and the same seat in each instance, in contradistinction to the endemic occurrence of tumors in man in which the tumors observed at the same locality had a usually different character in different individuals. I laid especial stress upon this difference between the endemic occurrence of cancer in man and in animals.

I furthermore found that if new rats were kept in the same cage with the rats which had been inoculated with tumors no spontaneous development of tumors was found, neither did the feeding of new animals with fresh tumors lead to a new formation of tumors in those rats. I pointed out the possibility that a hereditary factor is at the base of such endemic occurrence of cancer. I further concluded that if an infectious agency should be the cause of the endemic occurrence, the facts communicated render it very probable that tumors differing in structure and position are caused by *different* microörganisms.

In the following I intend to report on some further observations on the endemic occurrence of cancer in mice. In this case no certain proof could as yet be obtained of the infectious nature of the endemic occurrence; certain facts point even to the probability that hereditary influences are at work. In the latter part of December, 1906, I obtained from the same breeder six white mice which were affected with tumors. These tumors proved to be adenocarcinomas or carcinomas. Simultaneously three cages were received in which a number of mice affected with tumors had lived for some time. Approximately thirty white mice from a different source were put into those cages without any previous cleaning of the cages or without change of the bedding used for the tumor mice by the breeder. The new mice lived approximately three months in two of those cages[1] and no tumors developed among them. It can, of course, not be excluded that tumors may develop later. Personal inquiries made at the place where the tumor mice had been bred did not give any indication that the endemic occurrence could be attributed to certain infected cages. It appeared rather to depend upon hereditary conditions. The breeder believes to have observed cases in which a number of tumors were observed in different generations of the same family, although that family had changed cages repeatedly. Moreover, the cages were frequently washed. There was no special cage to which infection could be attribu-

[1] Medicine, April, 1900

[2] Centralbl. f. Bacteriol., 1904, vol. xxxvii.

[1] Most of the mice kept in one of the three cages were lost by accident about three weeks ago. Only three mice were saved. About a dozen new mice were added to the three old ones. April 2, among those mice, a female mouse with a tumor on the side was found.

ted. Tumors could be found in mice only eight months old. Many cases occurred in one small room and a few in the other small room. In each the mice were akin and considerably inbred, but unrelated or only very distant relatives of those in the other room. In each room they were bred two or three years with no change of stock except in the tumor-room, where at one time, new males all taken from one family, were introduced. The only difference in environment of mice in the two rooms was that in the tumor-room no sunshine was admitted, while the other was bathed in sunlight.

I now wish to give a somewhat detailed report of the tumors found in six mice which I received early in the winter of 1906-1907 from the breeder of mice referred to above.

1. *The first mouse* had a large tumor on the right side of the head and the upper part of the neck. The tumor was nodulated, somewhat hard, and had white, necrotic areas inside. No metastasis was visible to the naked eye. A little nodule was present, however, at the side of the large tumor on the neck. Microscopic examination showed the tumor cells, which were of an epithelial character, to grow usually in solid masses. The pressure of the cells upon each other caused them to be somewhat elongated. In other places, however, a distinct alveolar character was present, the central cells becoming necrotic or entirely dissolved, a central cavity being formed in this way. The colloid masses in the centre of the alveoli are much smaller than in the tumor of the second mouse and are of a different character. Wide areas of the tumor become necrotic; mitoses are present. Sometimes we find in the centre of the alveoli tumor cells which are much larger than the surrounding cells and have a large nucleus. Inside the alveoli these cells swell and may occasionally have two nuclei. Still later the nuclei and cytoplasma become dissolved. Sometimes a large number of tumor cells may swell simultaneously and degenerate, and then larger cavities are formed which are lined with tumor cells. In some places near the tumor we find collections of small mononuclear cells forming little packages. This tumor penetrates into the surrounding striated muscle and destroys it. At one place the tumor penetrates into the subcutaneous fat tissue. In a neighboring lympahtic gland a myeloplaque can be seen on microscopic examination; many mononuclear eosinophile cells are present in the fat tissue around the lymph glands. No tumor cells can be seen in this lymphatic gland. Macroscopically, the lung did not show any nodules. Microscopically, we find disseminated, in different parts of the lung, a number of tumor nodules which are of different size, but usually quite small. In the centre of some of the cell nests we find large, red-staining cells with a large vesicular nucleus. These cells probably form colloid material. Sometimes no lumen is visible in these cell nests; at other times an alveolar structure is present. These tumor cells are sometimes distinctly situated in the alveoli of the lung. No relation can be seen between the bloodvessels and the tumor nodules. This tumor was transplanted December 22, 1906, subcutaneously into thirteen rats. Besides, it was inoculated into tumor mouse No. 3.

Tumor mouse No. 3 inoculated with a little piece of tumor mouse No. 1 died thirteen days after the inoculation, January 5, 1907. Microscopic examination of the transplanted piece shows a necrotic mass in the centre. In the periphery, strings of tumor cells grow in large number. They at first form solid masses; through degeneration of some tumor cells a few small cavities are formed. In this way an alveolar appearance is occasionally produced in these cell masses. Some new-formed strings of tumor cells penetrate directly into the surrounding tissue without the preparatory work of any granulation tissue.

Another mouse examined, eleven days after the inoculation, showed a subcutaneous nodule with necrotic tissue in the centre. Tumor alveoli, in which the cells are a little shrunken, are present in the periphery of the necrotic mass. In the lung is found a nodule consisting of masses of epithelial-like cells filling out the alveoli of the lung. A neighboring bronchus shows adenomatous outgrowth. It is not certain whether this nodule in the lung was produced through the proliferation of the bronchial epithelial cells or through the proliferation of the alveolar epithelium of the lung. We certainly had not to deal with a proliferation of tumor cells which were inoculated directly from the first tumor mouse.

A third mouse inoculated with this tumor died twenty-six days after inoculation. A little subcutaneous nodule attached to the skin was found. This nodule consists mainly of necrotic tissue, but a few rows of tumor cells, which, however, are somewhat shrunken, are present.

2. *The second mouse* died suddenly during the night, in the latter part of December, and this tumor could, therefore, not be used for inoculation. The tumor, of about the size of a hazelnut, belongs to the type of papillary adenocarcinoma, in which the cells are usually much higher and the canals which they line wider and more irregular than in the other varieties of adenocarcinoma. The tumors form papillary prominences into the canals. Desquamation of masses of such cells into the lumen of the canal can take place, and their cytoplasm contributes to the formation of the colloid mass in the centre of the tubules. At one end of the tumor we find ducts and alveoli made up of smaller cells somewhat of the structure of the mammary gland. Some of the alveoli are lined by several rows of epithelial cells. At some places the tumor cells seem to penetrate into the fibrous connective tissue and to split the latter into smaller fibers. Some of these cells stain markedly with eosin. At other places part of the tumor cells form thin vacuoles in their cytoplasm and some alveoli can be lined by such finely vacuolar cells.

3. *The third tumor mouse* into which a piece of the first tumor mouse had been implanted, was found dead on January 5, thirteen and one-half days after the inoculation. Nine nodules, which were partly white, partly hemorrhagic, were found, mostly in the subcutaneous tissue in different parts of the body. These tumors were not used for transplantation. One subserous nodule was situated on the right side of the body near the thigh. It consisted of a dark, hemorrhagic, and a white, not hemorrhagic part. Microscopically the tumor consisted of alveoli containing some colloid material lined by one row of cells and of some more solid parts in which apparently the tumor cells were pressed closely together so that the alveolar arrangement disappeared. No mitosis could be seen; this may readily be explained if we take into consideration that the animal was dead for some time before the tumor was fixed. In the dense connective tissue near the ordinary alveolar tumor tissue there were gland-like, wider ducts which contained colloid masses. The latter had usually a concentric structure. This tumor nodule includes a lymph gland in the marginal sinuses of which large phagocytic cells can be seen which apparently take up lymphocytes. Another nodule was found between the right thigh and the genital organs. A part of this tumor was hemorrhagic. The alveoli here are a little larger and contain colloid. In the dense connective tissue we again find wide ducts with a dense colloid material. Parts of the tumor degenerated; in others hemorrhages were present. The tumor consists of alveolar and somewhat more solid masses of tumor cells. These more solid areas are merely tumor alveoli in which the cell proliferation has taken place more actively, and as a result of this proliferation the crowding of the cells takes place. This can be equally well observed in other tumors of this series. A third nodule was found in the subcutaneous tissue of the right humerus. This tumor appeared as a cyst with gray-white material inside. Microscopically large areas of necrosis were found in the centre. The fourth nodule was situated between the tail and the left thigh, subcutaneously. It was hemorrhagic and showed microscopically typical tumor structure with large degenerated areas. In the dense connective tissue we again find the gland-like cystic ducts containing colloid and lined by one row of flat cells. The tumor cells are here partially shrunken and large hemorrhagic areas are present. The lining epithelium of a cyst can be entirely lost at one side. The wall which separates two cysts can be perforated. The cytoplasm of desquamated cells is included in the colloid mass. There is much blood pigment present in the cells and in the colloid. A fifth subcutaneous nodule was found situated on the left side near the forearm and was partly necrotic. The tumor is, in part, degenerated and hemorrhages are visible under the microscope. In the dense connective tissue we again see balls of concentrically arranged colloid. The alveoli are somewhat shrunken. The sixth nodule, which was on the left side of the trunk subcutaneously, was very dark, a result of hemorrhage. There were also white parts present. This tumor had, in every respect, microscopically the same structure as the other nodules. The same colloid material was present in the ducts of the dense connective tissue. Much degeneration can be seen. Hemorrhages are present; in the peripheral sinuses of a neighboring lymph gland we see large phagocytic cells which have sometimes two nuclei. Even if these large cells in the lymph sinuses should be tumor cells, which is not probable, we would have to deal merely with a secondary invasion of the lymph glands inasmuch as the tumor nodule did not take its origin from a metastasis in the lymph gland. The seventh nodule was found under the skin of the neck. The nodule showed the typical microscopic structure. There were large areas of degeneration present. Again, in some of the sinuses of a neighboring lymph gland relatively large cells could be seen which originate probably through the proliferation of the endothelial cells, but their character as tumor cells cannot be entirely excluded. Near the spinal column three little transparent nodules were found. They showed the same structure; the glandular ducts filled with the colloid masses in the connective tissue could be seen. The colloid bodies are even visible between the striated muscle into which the tumor penetrates. A little lymph gland free from tumor is situated in the neighborhood of these three tumor nodules. Firmly attached to the skin a little nodule could be seen in the abdominal wall. Microscopically we here find necrotic material encapsulated by connective tissue. In the subcutaneous tissue nearby, glandular ducts which contain the typical colloid and alveolar granular tumor tissue are present. The largest tumor of this mouse had about the size of a walnut, and was situated near the left thigh. It was softer than the tumors of mouse 1 and 2 and was partly hemorrhagic. In the kidney of this animal a cyst was present, the contents of which could not be determined. In the lung nothing special could be seen.

4. *In the fourth mouse* the tumor was partly hemorrhagic and soft. The tumor consisted of simple alveoli which were arranged in rows between the bloodvessels. The blood channels are very wide and merely lined by endothelium. The small alveoli were separated by edematous connective tissue. A small number of mitoses could be seen. The structure of this tumor had some distant resemblance to that of a perithelioma. In other places of the tumor the alveoli without lumen are closely pressed toward each other. At such places there are more mitoses present and no dilated capillaries are seen. Wherever we find many mitoses, the connective tissue is not seen to be edematous; and where we find edematous connective tissue between the alveoli the mitoses are not very numerous. The lymph glands which were examined microscopically were found to be normal. In the lung, which appeared to the naked eye to be normal, small metastases

were found on microscopic examination. The tumor cells of the metastatic nodules had a somewhat alveolar arrangement but sometimes no distinct lumen was present. Some connective tissue surrounded the tumor nodules; small nodules of round cells were also present.

Twenty-one mice were inoculated with material from this tumor, on January 8. Thirteen days after inoculation one inoculated mouse was killed. Microscopically, a mass of necrotic tumor tissue was found which was surrounded by connective tissue.

5. *In the fifth mouse* one tumor was found situated on the left side of the chest near the leg; this tumor was very large and began to break through the skin; it was quite hard. On the right posterior part of the body a somewhat smaller tumor was found. It was a little softer and had not yet penetrated through the skin. No metastasis was visible to the naked eye. The tumor on the posterior part of the body, which had not yet broken through the skin, showed alveoli with or without red-staining colloid material in the centre. A few small areas were seen in which the cells were pressed together; some of these cells were in mitotic division, otherwise no mitosis could be seen. At places where the cells were pressed together, the alveolar character was no longer well pronounced. The tumor tissue can penetrate deeply into the neighboring tissue. In the fat, which surrounds the tumor, the blood capillaries are well visible and in the neighborhood of the blood vessels we see canals lined with high cells and with a colloid material in the centre. The alveoli of this tissue have a somewhat larger lumen than could be seen in the former tumors. Some areas of necrosis are present.

January 19 seventeen mice were inoculated with this tumor. Two days later one inoculated mouse died. In the centre of the nodule the section shows necrosis. In the periphery living tumor cells are present with well-preserved alveoli which are perhaps a little shrunken. Four and one-half to five days after the transplantation seven tumor mice died, probably as a result of exposure to cold. The transplanted pieces were examined microscopically. No. 1 was mostly necrotic. At the margin, tumor alveoli were present which were well preserved but somewhat shrunken. No. 2 shows the same picture. In some peripheral alveoli vesicular nuclei are well preserved. No. 3 shows the same. Especially noticeable is the fact that some of the transplanted alveoli, which were on all sides surrounded by connective tissue, were better preserved than some of the more peripheral alveoli. No. 4 shows, likewise, at the margin, alveoli which are well preserved and only a little shrunken. In No. 5 the same condition is found. No. 6 is almost entirely necrotic. At the margin a few shrunken alveoli are present. No. 7 is entirely necrotic.

The second tumor of mouse 5, which was a little ulcerated, shows in the whole the same structure as the first one. There are, however, more glandular ducts present in the connective tissue which separates the tumor lobules. The tumor lobules themselves are composed of large or small alveoli which contain a colloid mass in the centre. A number of mitoses are present in the tumor cells. Where the tumor cells are pressed together the mitoses are more numerous and at such places alveoli, containing a lumen, can hardly be seen. The tumor penetrates at certain places into the surrounding striated muscle and destroys the muscle tissue.

This tumor was transplanted, January 19, 1906, into thirteen mice. Three days after inoculation one inoculated mouse died. The greater part of the inoculated tumor was necrotic. At the margin, alveoli were present which were rather shrunken, but which were otherwise well preserved. No polynuclear leukocytes could be seen. Fourteen days after transplantation another mouse was found dead. The transplanted piece was entirely necrotic. The connective tissue penetrated into the necrotic material.

No metastases were found in the lung of mouse No. 5 on microscopic examination.

The sixth mouse had three tumors which were situated on the left side of the body between the anterior and posterior extremities. The tumor situated near the left hind leg developed only a few weeks after the mouse had been received. This last tumor was quite hemorrhagic and was not used for transplantation. The tumor situated anteriorly contained much dark, hemorrhagic fluid. Part of it was used for transplantation. The second tumor was not hemorrhagic. Microscopically this tumor was found to consist of small alveoli with a lumen in the centre; besides there were present more solid parts in which no lumen was visible between the cells. Both parts showed mitoses, but they were more numerous in the more solid parts. The structure of this tumor was almost identical with that of the tumors of the third mouse. Ducts lined with several rows of epithelium were also present. Mitoses could be found in the cells lining these ducts. At some places, however, the ducts were lined with only one row of epithelium.

One white mouse and two gray mice were inoculated with material from this tumor.

The second tumor of this mouse was not hemorrhagic. Microscopically, we find masses of densely-packed cells with mitoses. Usually no lumen is visible between the cells. At other places, however, distinct alveoli with a lumen in the centre are present. In the connective tissue glandular ducts can be seen. The structure of the first tumor differs from the second tumor by the prevalence of the densely packed cells and the smaller number of well-formed alveoli. The difference between the first and second tumor depends mainly upon the large amount of densely packed cells in the second tumor.

A piece of this tumor was inoculated into seven white mice, three of which were pregnant on January 23. At the same

time ten white mice were inoculated with tumor material which had been heated previously for an hour to 39°. One of the pregnant mice died two and a half days after inoculation. Microscopic examination showed the transplanted piece to be almost entirely necrotic. In the periphery there are areas of shrunken, partly disorganized tumor cells. In a mouse killed two days, seventeen hours after inoculation, the inoculated piece showed necrotic material in the centre. In the periphery there were some well-preserved ducts present, the cells of which were only little altered or shrunken.

The third and more recent tumor was very hemorrhagic. Very irregular, degenerated areas can be seen in this tumor. As a result of the degeneration, large cavities are formed. Many hemorrhages are seen in the sections. Mitoses can be found in the tumor cells. In the fat tissue surrounding the tumor, gland-like ducts which form a part of the tumor tissue are visible.

The third tumor seems to have originated in a fat lobule in which the tumor cells form gland-like ducts, and which proliferate as is indicated by the presence of mitoses. In the centre of the ducts concentrically laminated colloid masses can be seen. At one place in the fat lobule a collection of lymphoid cells is present. In the axillary lymphatic glands we find marked proliferation of the endothelial cells of the sinuses. In the lungs little nodules are formed by collections of round cells on the pleura. Near such epipleural nodules in the lung tissue, other proper nodules are formed through a proliferation of alveolar epithelium. A round, cyst-like body which was cut almost entirely into serial sections, and was found to consist of tissue closely resembling the structure of the body of the epididymis, was discovered in the axilla of this mouse. Desquamated cells and some rod-like bodies which resembled spermatozoa could be seen in the lumen of the canals. No trace of the testicle was present. Instead, we found areolar connective tissue. The arrangement of the ducts around this areolar tissue was very similar to that of the epididymis around the testicle.

It will now be necessary to discuss some of our observations and experiments with reference to conclusions reached by other investigators. We found indications that the endemic occurrence of cancer is, in part at least, caused by hereditary conditions. Certain predisposing conditions transmitted to different members of the same family may be one of the factors which determines the endemic occurrence of cancer. On the other hand, no definite indication could be obtained tending to prove that the presence of an organism in the cage was responsible. The cages were frequently cleaned. The mice in different rooms were kept in the same way. They were given the same food. Their cages were cleaned by the same person. Nevertheless, the endemic occurrence of cancer was mainly confined to one room. The mice kept in this room belonged to a certain number of families which interbred among each other, but were kept entirely separate from mice in the other room. There are indications that young mice descending from the same parents developed tumors although they were kept in different cages. If we, therefore, have facts which suggest that hereditary influences are important, we cannot ignore certain observations made by other investigators which suggest very strongly that transmission of a microörganism is responsible for the endemic occurrence of cancer among animals. Here we must mention the observations of Morau,[1] who believes that certain insects carried the infecting organism from one mouse to another and were thus responsible for the endemic occurrence observed in his cages. Recently Haaland[2] reported from the Institut Pasteur, observations which seem equally to suggest a microörganism as the cause of the endemic occurrence of cancer in mice. It was found that if mice afflicted with cancer were put into cages containing mice obtained from places at which no cancer had been observed in the course of a year, cases of cancer developed among the mice which had been hitherto free from tumors. On the other hand, if they put mice which were free from tumors into cages in which a number of tumor mice had been raised, tumors could not be observed to originate among the new mice if the tumor mice had been removed before the new mice had been put into cages. Very interesting are the recent observations of Gaylord and Clowes.[3] Toward the end of the third year of my transplantations of the cystic sarcomas of the thyroid of rats, a number of rats affected with sarcoma were kept for several months in some cages in the New York State Cancer Laboratory in Buffalo. Two years after my rats had been removed, another rat which had a fibrosarcoma of the right abdominal aspect was found in one of the cages previously inhabited by my rats. A little more than a year later two other sarcomas were detected among new rats kept in the same cages. One of those was a fibrosarcoma on the right side of the abdominal aspect. The other was a cystic sarcoma of the thyroid region. This observation is certainly very striking and suggests the transmission of microörganisms as a cause of the endemic occurrence of cancer. As yet we cannot, however, regard this explanation as absolutely proven, inasmuch as the sarcoma of the thyroid of rats is found at different places in America. At least, I myself obtained a rat affected with sarcoma of the thyroid which was found in the laboratory of an insane asylum in Iowa. The other sarcomas of the thyroid of rats which I have used in my experiments were obtained from a different source in Chicago.

[1] Recherches expér. sur la transmissibilité de certains neoplasmes. Arch. de médec. expér., 1894. I could not find any statement in the original papers of Morau regarding the action of insects. If it should exist, it must have escaped my notice. Several writers, however, as E. G. Borrel, mention the views of Morau.

[2] Les tumeurs de la souris, Annales de l'Institut Pasteur, 1905.

[3] Evidences of Infected Cages as the Source of Spontaneous Cancer, Jour. Amer. Med. Assoc., January, 1907.

In Europe, Velich found a fibrosarcoma situated on the leg of a rat. Firket, and v. Eiselsberg likewise found sarcomas in rats. Nevertheless, it is not likely that the observations which indicate the transmission of a microörganism as the cause of the endemic occurrence of cancer in animals are to be explained as accidental occurrences, and it is possible that several factors are active in producing the endemicity of malignant tumors. Morau,[1] on the other side, also found indications of a hereditary transmission of carcinoma in mice. Eberth and Spude[2] found tumors in several mice of the same family. They interpret this occurrence evidently as due to a hereditary disposition. It is, however, doubtful whether in

Fig. 1.—Mouse 6 with three tumors. The third tumor developed shortly before the death of the animal.

their case the influence of microörganisms can be excluded with certainty. Doubtful also is the interpretation of the endemic occurrence of carcinoma of the thyroid gland found in the trout and which was recently very carefully described by L. Pick.[3] Fish kept in certain tanks acquire this disease, which in this case is not limited to fish of the same family; if heredity plays any part at all in this case, it is certainly not the only important factor. On the other hand, Pick does not bring forward any fact which excludes the possibility of an infectious origin. He thinks it most probable that the primary condition present in the trout is struma of the thyroid. He believes, in fish as in man, goitre to be caused by certain conditions of the water and to occur endemically. The occurrence of carcinoma is then merely a secondary condition following the goitre. He believes that there is as little cause to assume a microörganism as the cause of carcinoma of the thyroid of the brook trout as it is in the case of the endemic occurrence of goitre in man. From these different observations we might, in a tentative way, draw the conclusion that several factors cooperate in the causation of the endemic occurrence of cancer in animals. A further elucidation of those factors promises results of great importance for the understanding of the cause of malignant tumors in general.

Our observations recorded above are of interest in some other respects. In the first place, we find that among six mice affected with spontaneous tumors, and being sent by

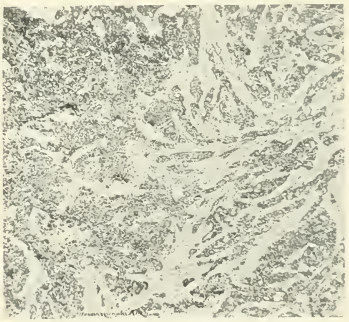

Fig. 2.—Section through tumor of first mouse. The tumor consists mostly of solid masses of cells. At some places an alveolar arrangement is visible.

the same breeder, three mice had multiple tumors. One mouse had two, another mouse had three, and the third mouse nine at different parts of the body. Of these three mice, two had been kept longer in the laboratory than the others. It is quite possible that multiple tumors would have developed in some of the other mice, if they had been somewhat longer under observation. In one case at least it was distinctly possible to follow the development of a new tumor in a mouse previously affected with two other tumors. Picture No. 1 shows mouse 6 with three tumors. The one situated posteriorly was not present when the mouse was sent to Philadelphia. It seemed to develop quite suddenly and appeared at first to be in close proximity to the second of the three tumors.

These observations show: first, that we have here to deal with an endemic occurrence of so-called multiple tumors; secondly, that the structure of the tumors which were multiple

[1] Morau, C. R. Académie des sciences, 1893.
[2] Ueber familiare Endotheliome, Virch. Archiv, Band cliii.
[3] Berl. klin. Woch., 1905, vol. xlii.

(tumors in mice 3, 5, and 6) was not identical but very much alike, much more so than the structure of the tumors found in mice 1, 2, and 6, which differed in some respects from each other, and from the tumors of the other set of mice. The multiple tumors, which were present in different mice, were almost identical in structure in the same mouse. Some minor differences were probably due to some accidental conditions such as hemorrhage. There exists, therefore, an endemic occurrence of multiple tumors. Whether this endemic occurrence of multiple tumors is due to the predisposition of the animals affected, or whether it is due to a special character of the tumor, cannot be determined at present, but it is hoped that transplantation of these tumors may answer this question. Another question arises, however: In this case do we have actually to deal with multiple primary tumors or are those tumors secondary metastases of one primary tumor into

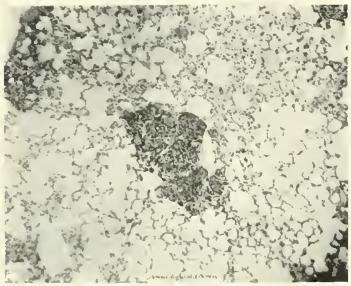

Fig. 3. Metastasis in the lung of mouse 1.

the subcutaneous tissue, or into the tissue adjoining the latter? It is certainly an unusual thing for carcinoma to cause the formation of multiple metastases rather at distant places in the skin than in the internal organs. Furthermore, we could not find any evidence of metastases in the lymph glands. In not a single instance was there any indication that one of these multiple subcutaneous tumors originated in a lymph gland. The lymph glands were in each case free from tumors. There were cells visible in the sinuses which were probably proliferated endothelial cells or mononuclear leukocytes. We would, therefore, have to assume that the metastases took place through the bloodvessels. It would, however, be hard to explain why the bloodvessels should carry tumor cells into other parts of the skin rather than into the internal organs, which is the ordinary situation of metastases in carcinoma.

The multiple subcutaneous tumors are scattered over very wide areas of the body, and they are found at such places where the existence of normal mammary-gland tissue can with great probability be excluded. We have, therefore, the following alternative: Either we have to deal with multiple metastases into the subcutaneous tissue, a very unusual occurrence for carcinoma if the dissemination by the lymphatics can be excluded, or we have to deal with a real multiplicity of primary tumors. In the latter case it becomes very unlikely that all tumors take their origin from the mammary glands. Such an origin would, for instance, be extremely unlikely in the case of the little tumor which was found directly at the side of the root of the tail, or in the case of the nodules found near the spinal column. Careful studies led especially Apolant to the conclusion that all subcutaneous adenocarcinomas of the white mouse take their origin in the mammary gland. The description of Apolant leaves no doubt as to the great similarity of these tumors in American and in European mice.

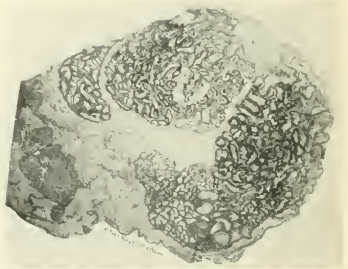

Fig. 4. Section through a body resembling the epididymis, found in axilla of mouse 1.

Macroscopic metastases into inner organs could not be seen in any of the mice, but on microscopic examination small metastatic nodules could be found in mice No. 1 and 4; two animals in which no multiplicity of tumors existed. The metastases in the lung consist of very small disseminated lobules which at first are almost free from connective tissue, the tumor cells growing into the alveoli. Later, the tumor nodule is invaded and surrounded by connective tissue. The way by which the lung is invaded cannot be clearly seen. Emboli of tumor cells are not visible in the pulmonary vessels. Haaland was able to demonstrate the presence of microscopic metastases in cases in which macroscopically no metastases were present. We could likewise confirm another observation of Haaland's. We found that in the lung of mouse No. 6, besides the epipleural nodules of lymphoid cells and of proliferated pleural endothelial cells, nodules were present which seemed to consist of proliferated alveolar epithelium. In a similar way in a mouse inoculated with the tumor of mouse No. 1 which died eleven days after inocula-

tion, a little nodule was found in the lung which consisted of proliferated epithelium of an adjoining bronchus or of the epithelium of the alveoli of the lung. Such tumor-like formations cannot be regarded as due to metastases of tumor cells; it will, however, be advisable to suspend judgment about their significance until further control examination of lungs of normal mice, and of the lungs inoculated with other than tumor material, have been made.

Our tumors infiltrated the surrounding muscle and fat tissue in a similar way as does carcinoma in man.

Of especial interest is the fact that in the axilla of mouse No. 6 which had several spontaneous tumors, and which, like the other mice, was a female, we found a round body the structure of which closely resembled the epididymis. In this connection it may be stated that in two mice which we received from another breeder I found cysts situated at the neck of the animals. These cysts were lined by cuboidal

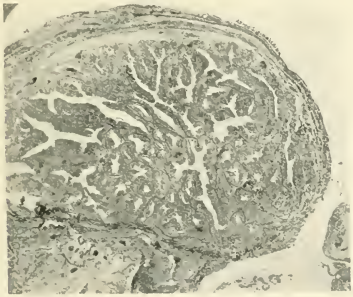

FIG. 5. Section through adenocarcinoma of mouse 2. Papillomatous structure. No colloid material present in this part of the tumor.

epithelium and contained a fluid. One of these two cysts, which was under observation during several months, enlarged gradually, until the cyst ruptured subcutaneously and its contents escaped. The wound closed and the cyst began to fill again. Transplantation of parts of the cyst wall into other mice did not lead to the formation of new cysts. The same breeder who sent these two mice to the laboratory has supplied us with two mice which were affected with adenocarcinomas; in one animal the tumor was situated in the subcutaneous tissue of the neck, in the other it was attached to the thigh. One of these tumors was transplanted successfully. We see, therefore, that in mice which are either themselves afflicted with tumors or in mice bred at places where tumors are occasionally found among other mice, certain peculiarities occur which, in part at least, may be due to congenital malformation.

Inoculations with the tumors found in four mice were carried out into a very large number of other white mice. A number of these animals died accidentally from exposure to cold. The transplanted pieces were examined microscopically. An active proliferation of inoculated tumor cells could not be seen on microscopic examination, with the exception of one case which shall be referred to shortly. Of all the mice which remained alive, only one developed a tumor. The one mouse in which, on microscopic examination, the development of a tumor was seen in the periphery of the inoculated piece was in the case of tumor mouse No. 3 which had been inoculated with material from the tumor mouse No. 1. This mouse died thirteen days after it had been inoculated. I was led to inoculate a mouse which carried a spontaneous tumor by the consideration that animals already affected with a spontaneous tumor might be a more favorable soil for the growth of an

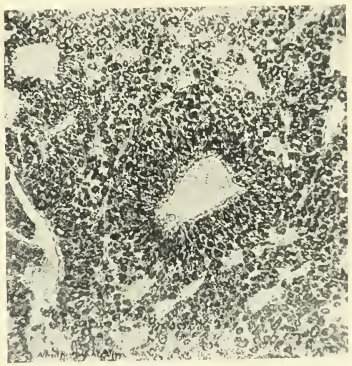

FIG. 6. Section through tumor (adenomatous part of an adenocarcinoma) of mouse 1. Perithelioma-like arrangement of the alveoli. Blood capillaries are much dilated.

inoculated tumor of a similar character. An experiment done, approximately six years ago, in which I transplanted an adenoma of the mammary gland of a rat simultaneously into other rats, and into the rat affected with the tumor demonstrated the great difference between the fate of the transplanted piece in the rat affected with the tumor and in other rats. In the latter the piece very soon degenerated; in the former it was preserved and enlarged even during pregnancy. In this case the pregnancy of the animal may have been a complicating factor. Such a complication did not exist in the recent experiment. The fact that the mouse carrying the spontaneous tumor was successfully inoculated with a tumor of another mouse and that, on the other hand, among all the other inoculated mice only one single mouse developed a tumor, is hardly an accidental occurrence, but seems to

demonstrate that there exists a certain relationship between the predisposition of the animal which favors the development of a primary tumor and that kind of predisposition which permits transplanted tumors to grow. Experiments carried on with Dr. S. Leopold on a carcinoma of a mammary gland of a dog during the winter 1906–1907 showed equally well that the pieces of tumor transplanted into the animal originally affected with the tumor may remain alive, although pieces transplanted into other dogs became necrotic.

In my first papers on the experimental inoculation of tumors I carefully distinguished between these two sets of factors. The experiments recorded here suggest that after all there exists a connection between these two factors and that some of the conditions which permit transplanted tumors to develop are identical with or related to some of those conditions which contribute to the development of a primary tumor in an animal. This predisposition is, however, only one of the factors which participate in the production of a primary malignant tumor in an animal.

One more conclusion, as to the inoculability of tumors, may be drawn from these experiments, namely, that multiplicity of tumors does not necessarily correspond to a high degree of inoculability of such tumors into other animals. In a former paper[1] I pointed out another condition, namely, that a connection between the rapidity of growth of the primary tumor and the inoculability of tumors does not need to exist. Tumors which grow relatively slowly in the original mouse and in the first generation of inoculated mice may, nevertheless, yield 100 per cent. of successful inoculations, and rapidly-growing tumors, on the other hand, may only be inoculated with great difficulties. The inoculability of tumors depends, therefore, on a number of different conditions, and the energy of growth of the original tumor is merely one of the factors which are of importance. It is only by careful experimental analysis of the different factors which determine the growth of tumors that we hope to come nearer to a full understanding of the direct cause of tumors. We have to be satisfied to add one small piece of evidence to another. The difficulty of obtaining sufficient material favorable to experimentation excludes, in many cases, the carrying on of as large a number of experiments as could be desired.

[1] Zeitschr. f. Krebsforschung, vol. v.

Some of the observations and conclusions may be summarized as follow :

1. The observations recorded here suggest that hereditary transmission of certain predisposing conditions from parents to offspring is one of the factors causing the so-called endemic occurrence of cancer among animals.

2. It is shown, experimentally, that various kinds of tumors remain better preserved when inoculated into the animal in which the tumor had developed originally, or into an animal affected with the same kind of tumor than when inoculated into other animals of the same species. In the latter they may become necrotic; in the former they remain alive or grow. This has been found in three sets of experiments in the rat, mouse, and dog. Further experiments must determine to what extent this rule generally holds good.

3. No parallelism need to exist between the tendency of tumors to become multiple and their inoculability into other mice. Originally slowly growing tumors may be easily inoculable. The energy of growth of the original tumor is only one of the factors which determines the degree of inoculability of a tumor.

4. An endemic occurrence of multiple tumors among mice is described. As many as nine tumors may be found under the skin in different parts of the same mouse. The tumors found in the same animal are almost identical. If these tumors represent primary multiple tumors and not metastases, the conclusion is inevitable that many of these tumors are not derived from the mammary glands. Metastases into lymphatic glands could never be found.

5. In confirmation of Haaland's observations, microscopic metastases can be found in the lung in a certain number of cases when macroscopically no metastases exist. Besides the metastatic nodules, different nodules are occasionally formed in the lung through the proliferation of the alveolar or bronchial epithelium.

6. An unusual anomaly is described in a mouse affected with a tumor. A structure closely resembling the epididymis was found in the axilla of a female mouse. Other mice sent by a breeder, among whose stock tumors had been found, showed in each case the development of a large cyst in the neck. The possibility of a relationship of these anomalies to the formation of certain tumors in mice must be taken into consideration.

INTERNAL HYDROCEPHALUS.

With Report of Two Cases, One Resulting from Occlusion of the Aqueduct of Sylvius.[1]

By William G. Spiller, M.D.,
Professor of Neuropathology and Associate Professor of Neurology in the University of Pennsylvania,
and
Alfred Reginald Allen, M.D.,
Assistant in Neuropathology in the University of Pennsylvania.

(From the Department of Neurology and the Laboratory of Neuropathology in the University of Pennsylvania.)

It is by no means rare to find occlusion of the aqueduct of Sylvius as one of the etiological factors in internal hydrocephalus mentioned in text-books dealing with this subject. Attention is particularly attracted by the fact, however, that no references are given, in most of the articles which refer to this occlusion as a possible cause, whereby one can determine that the author is speaking from clinical experience and not theorizing.

We have been struck with the *a posteriori* nature of discussions on this subject, and it is therefore with pleasure that we bring forward a case of internal hydrocephalus the cause of which is probably congenital, almost total occlusion of the aqueduct of Sylvius.

Anton,[2] in dealing with the causes of hydrocephalus, quotes Baginsky's opinion that acute hydrocephalus is identical with acute non-tuberculous inflammation of the choroid plexus and the following increase of exudation. He adds that there is without doubt involvement of the ventricle walls and the ependyma. He also advances the view held by Rindfleisch, Huguenin, and von Bönninghaus to the effect that the inflammatory affection of the ventricles and choroid plexus is always associated with a meningitis serosa or purulenta, and that these are caused by toxic or infectious factors. Referring to Macpherson, he states as a possible cause an infectious phlebitis with thrombus formation of the venous sinuses. He says that occasionally the exciting agent of the inflammation gains access directly to the ventricle through the brain substance, with or without traumatism, and there sets up a fibrinopurulent process. Lastly, he calls attention to a possible connection between rachitis and hydrocephalus.

Gowers[3] holds that the "only known cause" of acute hydrocephalus is meningitis. Speaking of chronic internal hydrocephalus he makes this interesting statement: "Sometimes all the ventricles are distended; more often the fourth ventricle suffers little, even where there is no obstruction in the aqueduct of Sylvius. In such a case the aqueduct may be funnel-shaped, dilated toward the enlarged third ventricle." This statement should be compared with the gross anatomical findings of our second case. Gowers further mentions the possible obstruction of the veins of Galen preventing the return of venous blood from the intraventricular vessels and thereby becoming a cause. Such a condition as this, if acute, is likely to cause ventricular hemorrhage and rapid death, as in a case reported by one of us (Spiller) with Wadsworth, but when developing slowly might be productive of internal hydrocephalus.

Oppenheim[4] speaks of compression of the aqueduct of Sylvius as a cause of internal hydrocephalus. D'Astros[5] states that an obstruction of the aqueduct of Sylvius will produce *une hydropsie* of the third and lateral ventricles; but he gives no instance of its so doing. A Henle[6] says that a closure of the aqueduct of Sylvius will cause a hydrocephalus confined to the third and lateral ventricles; but he gives no reference to a case. P. Bourneville[7] speaks of "another case" of hydrocephalus caused by the obliteration of the aqueduct, but no further information is given. F. Schultze[8] mentions the possibility of hydrocephalus being caused by the obstruction of the aqueduct, and refers to Seeligmüller's cysticercus case which we cite below.

Seeligmüller[9] speaks of a possible pressure on the aqueduct of Sylvius by a tumor causing hydrocephalus. In the same work he gives the history of his case of hydrocephalus caused by the plugging of the aqueduct by a cysticercus the size of a cherry stone. Apropos of cysticercus Karl Osterwald[10] has collected about 34 cases in literature of cysticercus in the ventricles of the brain, but in none of the cases given was the parasite in the aqueduct.

[1] This article also appeared in the Journal of the American Medical Association, April 13, 1907.

[2] Flatau-Handb. path. Anat. d. Nervensystems.

[3] Dis. of the Nervous System.

[4] Lehrb. d. Nervenkrankheiten.

[5] Les Hydrocéphalies, 1898, 75

[6] Beitr. z. Path. u. Therap. d. Hydrocephalus.

[7] Brouardel, Traité de médecine.

[8] Nothnagel, Specielle Pathol. u. Therap.

[9] Krankheiten d. Rückenmarks u. Gehirns.

[10] Beit. z. d. Diag. Cysticercus Ventriculi Quarti, Neurolog. Centrbl., March 16, 1906.

Bönninghaus[1] gives as a cause of hydrocephalus, what he terms an "acute automatic closure" of the aqueduct of Sylvius. By this he means that when the effusion into the third and lateral ventricles occurs rapidly, the more yielding portions of the third ventricle, *i.e.*, the floor and the roof, become displaced and pull from above and below on the more solid pons, and in this way produce an elongation of the aqueduct which may result in complete closure.

One of us (Spiller[2]) reported a case in which the third and lateral ventricles were dilated and the aqueduct was occluded by proliferation of the neuroglia. Two other cases of partial internal hydrocephalus have come under his notice. In one the distention was confined to one lateral ventricle of the brain and was caused by partial inflammatory closure of the foramen of Monro; in the other case only the posterior horn of the lateral ventricle was distended, and very greatly, from unknown cause. In this case the occipital lobe of the affected side was a mere sac. He also refers to a case of Bourneville

Fig. 1.—Photograph of one cerebral hemisphere, showing the great distention of the lateral ventricle and the thinness of the brain tissue.

and Noir[3] in which the aqueduct was entirely occluded, but there was no microscopic study of the tissues. In this same paper he (Spiller) speaks of Touche's case,[4] in which there was occlusion of the aqueduct.

Our attention has been called by Dr. H. E. Becker, of Quincy, Ill., to a case of occlusion of the aqueduct reported by Hilton in his *Lectures on Rest and Pain*. The sections from still another case (unreported) have been shown us by H. S. Hutchinson.

Our first case was reported by one of us (Spiller) without microscopic study.[5] The history as obtained from the Pennsylvania Training School for Feeble-minded Children is as follows:

Patient. Sally H., aged sixty-two years at time of death; American.

History. Father died of consumption, aged thirty-nine years; mother died aged sixty-three years, cause unknown; two brothers and two sisters died of consumption. One sister (the first born) died in early infancy, cause unknown; two brothers are living in good physical and mental condition. Of the details of the patient's birth nothing is known. She was supposed to have been born hydrocephalic and was weak and sickly as a baby. Sight, hearing, and speech were good. She had epilepsy for years and during her seizures would froth at the mouth and purge. She suffered frequently from vomiting without assignable cause, and had occasional attacks of vertigo. She was said to have chronic kidney disease six years prior to her death. There was no paralysis at any time, and although no joint complication was

Fig. 2.—Photograph of a child, aged one and a half years, with intense hydrocephalus.

present she always walked as though lame. She was said by Dr. Llewellyn, who had known her for years, to have been fairly well developed mentally. Her advanced age and her mental condition are remarkable in view of the extensive hydrocephalus.

Macroscopic Examination. The third and lateral ventricles of the brain were greatly dilated and the white matter surrounding them was intensely atrophied. The whole cerebrum appeared as a greatly distended sac. The lateral ventricles freely communicated with one another, and the walls of the third ventricle were so pushed apart that the floor of this ventricle was on a level with the upper part of the basal ganglia.

Microscopic Examination. Left optic thalamus: The blood-vessels were thickened and there were some recent hemorrhages within the substance of the thalamus. All the vessels were distinctly congested. There was little vacuolation of

[1] Die Meningitis Serosa Acuta, 1897.
[2] Amer. Jour. of Med. Sci., July, 1902.
[3] Le progrès méd., July 14, 1900, 17.
[4] Bull. et mémoires de la Soc. méd. d. hop. de Paris, 1902, xix, 141.
[5] Jour. of Nervous and Mental Dis., 1900, 559.

the cells of the choroid plexus such as described by Raubitschek.[1]

Corpus callosum: A section from the median portion of this structure was not more than 1 mm. in thickness; it stained normally and contained numerous amyloid bodies.

Left occipital lobe: In places the cortex and white matter were not more than 2 mm. in thickness; in other places the thickness was 6 mm. The atrophy was relatively much greater in the white substance than in the cortex. Where the width of the section was the least, more than half was occupied by the cortex. The cells were much diminished in number, as shown by the thionin method.

The fornix: This was much atrophied and the bloodvessels within it were greatly thickened.

The aqueduct was almost occluded, this occlusion being probably a congenital malformation because the cavity was well lined throughout by a layer of ependymal cells, which would hardly be the case if the occlusion were caused by proliferation of the neuroglia. The neuroglia tissue immediately adjoining the ependymal lining was a little proliferated, and the aqueduct was filled with red blood corpuscles which were unaltered in shape, and probably were deposited there shortly before death. To the naked eye the aqueduct seemed to be entirely occluded. In a microscopic section the aqueduct to the naked eye was hardly as large as the point of an ordinary pin.

[1] Ztschr. f. Heilkun., 1905, p. 219.

The second case is reported as one of intense congenital hydrocephalus without occlusion of the aqueduct. The pathological material was received from Dr. Thompson S. Westcott, to whom the case belongs. The patient lived to be a year and a half old. The skull was excessively large. It is difficult to describe the gross appearance of the brain other than to say that it was a large, thin bag of nerve tissue so attenuated in many places as to be translucent, and the mere handling of it caused numerous tears in its substance.

Microscopic Examination. The corpus callosum was not more than 0.5 mm. thick.

Left occipital lobe: Sections in places were not more than 1 mm. thick. Here, as in the other case, the atrophy was much more pronounced in the white matter than in the cortex.

Left motor area, median side: The white matter was most affected. There was great diminution in the number of cells and the pericellular spaces were all distended. The cells appeared all decidedly smaller than normal. The pia was not thickened and the cortex and white matter were 4 mm. thick.

In contrast to the other case the fourth ventricle was greatly dilated as the result of the dilatation of the aqueduct of Sylvius. The cause of the hydrocephalus in this case could not be determined, but the condition seemed to have been a congenital malformation.

The two cases show very clearly that the distention of the fourth ventricle may depend on the patulency of the aqueduct of Sylvius.

ABNORMAL CONTRACTION OF THE EYELIDS IN ASSOCIATION WITH MOVEMENTS OF THE JAW.[1]

By Wm. Campbell Posey, M.D.,
Ophthalmologist of the Department of Physical Education, University of Pennsylvania.

F. R., a Hebrew girl aged seventeen years, came to the Polyclinic Hospital, complaining of dizziness and headache after near work. These symptoms had been present at intervals for several years, but she had never worn glasses or received other ocular treatment. She said that the right lid had dropped from birth, and it was further elicited that since earliest childhood it had been remarked that when she chewed or rotated her jaw the lid of the right eye would move up and down. It had also been remarked that her right eye would deviate upward at times, remaining in that position for several minutes. Her health had always been good. As far as she knew, no other members of her family had ever had drooping lids or the peculiar movements just referred to.

[1] Read before the Ophthalmological Section of the College of Physicians of Philadelphia, January 15, 1907.

Upon examination, with the eyes in the primary position, the lid of the right eye was seen to be in a state of marked ptosis, the upper two-fifths of the cornea being covered by it; the lid of the left eye was normal. The ocular movements were good and unrestricted in both eyes, except it was plainly remarked that when the eyes were directed up the right eye rose rapidly, higher than the left, *indicating an apparent over-action of the right superior rectus muscle.* The ptosis upon that side remained the same during this excursion. A study of the double images showed insufficiency in the right inferior rectus muscle, but all the other extra-ocular muscles functioned normally. Nor was the iris or ciliary muscle affected in either eye, for the pupils responded equally and freely to light and accommodation stimuli, and accommodation was normal. Vision equalled $\frac{2}{3}$ in each eye, both eyes being slightly hypermetropic. There were no changes in the fundi.

When the patient was given a piece of gum and asked to chew, up and down movements were observed in the right upper lid, which were synchronous and rhythmical with those of the jaw. The eyeballs, however, remained quiet, although this movement in the lid could be demonstrated at all times by the slightest rotation of the jaws. No motion was communicated to the lid by simply opening the mouth, nor were the eyeballs themselves affected by this act. The tongue was extruded straight in the median line and there were no palsies of the muscles of the face.

The case which has just been reported is an example of a rather rare class in which movements of the eyelid are influenced by those of the jaw. In the cases which have been

Fig. 1.—Associated movements of head and jaw, showing ptosis of right lid with overaction of right superior rectus when looking directly up.

recorded thus far this peculiarity is limited to one eye, and in the majority there has been observed a ptosis of greater or less degree upon the affected side. An excellent exposition of the subject can be found in Wilbrand and Saenger,[1] but as the condition is unusual it may perhaps not be amiss if I review very briefly the chief characteristics of this anomalous association.

Sinclair, who observed six cases and wrote an analytical paper upon the subject in 1895, grouped his own cases, with those in the literature at that time, into three series, the first comprising those in which certain movements of the lower jaw are associated with an upward movement of the upper eyelid. In this class, which Sinclair found to be the most commonly met with, there is one-sided, congenital ptosis, varying in degree, and with or without paresis of the superior rectus. The drooping eyelid cannot be voluntarily raised, but it is vigorously raised when certain movements of the lower jaw occur. The movement is strictly limited to the upper eyelid (levator muscle) and the patient cannot control it. It is best seen when the gaze is directed downward and the jaws are moved as in ordinary mastication of food.

Sinclair further subdivided the cases in this series into four sub-groups.

Fig. 2.—Associated movements of head and jaw, showing ptosis of right lid with overaction of right superior rectus when looking up and to the right.

Group I.—Cases of one-sided congenital ptosis in which the drooping eyelid is raised both when the mouth is opened (digastric) and also when the jaw is directed to the opposite side (external pterygoid).

Group II.—Cases of one-sided congenital ptosis in which the drooping eyelid is raised when the jaw is depressed, but is not raised with lateral movements of the jaw.

Group III.—Cases of one-sided congenital ptosis in which the drooping eyelid is raised with lateral movement of the jaw (external pterygoid action), but not with simple opening of the mouth.

Group IV.—Cases in which similar associated movements

[1] Vol. 1, p. 60.

of one upper eyelid with movements of the lower jaw occur, but in which there is no ptosis.

Of the 32 cases analyzed by him, ptosis was present in 27 instances and doubtful in 1, and of the 27 cases in which ptosis was present the superior rectus was paretic in 10.

Block has reported an instance where the condition was hereditary, occurring in two sons whose father died of brain tumor.

In a case reported by Uthoff there was palsy of the rectus internus, and Vossius observed two brothers in whom the eyes had been completely immobile since birth. The eye in Hubbel's case was divergent and amblyopic, and there was limitation of action of both superior and inferior recti muscles. Fuchs, Just, Fränkel and Wilbrand and Saenger have observed cases of associated movements between lid and jaw where ptosis and other congenital anomalies were absent.

Although the condition is generally regarded as being congenital, Friedenwald describes a case in which the movements did not appear until the patient was fourteen years old, and while, as a rule, the movements remain unchanged throughout life, they may in certain cases become more pronounced and in others less, so that the prognosis as to the permanency of the anomaly in its condition present at the time of examination cannot always be assured.

The explanation of the association is difficult and must be purely hypothetical, as no cases as yet have come to autopsy. The theory which is usually accepted is that proposed by the committee which was appointed by the Ophthalmological Society of the United Kingdom to report upon Marcus Gunn's case, which was the first recorded in ophthalmic literature. This was to the effect that the levator receives nerve supply from the motor nuclei of the fifth nerve as well as from the nuclei of the third. Others have thought of a nuclear connection between the third and seventh nerves, and there are still others who presuppose a connection between the nuclei of all three nerves. While there is ground for belief in the imperfect development of the third nerve nuclei in a number of the cases, as is evidenced by insufficiency in the action of superior and inferior rectus and other muscles supplied by that nerve, this is not true of all, for, as has been stated above, other cases have been cited where all the muscles supplied by this nerve performed their functions normally, the associated movements between the lid and jaw being the only anomalous conditions present.

PECULIAR TYPES OF GANGLION CELL DEGENERATION.

By D. J. McCarthy, M.D.,
George B. Wood Professor of Medical Jurisprudence, University of Pennsylvania.

(From the William Pepper Clinical Laboratory, Phoebe A. Hearst Foundation, and the Laboratory of the Henry Phipps Institute.)

With the study of the finer anatomy of the ganglion cell, following the application of the methylene-blue stains to nervous tissues many contributions of value have been made to the anatomy of degeneration of ganglion cells. The Nissl method and other modifications of the use of methylene blue as used by Nissl served a purpose in calling attention to the presence of areas in the cell protoplasm outside of the nucleus, taking the basic stain intensely, and to which was given the name of chromophilic elements. Much has been written as to whether these areas are artefacts produced by the fixing process, or, as some maintain, by the section of acid agents on the cell substance. If sections of nervous tissues be made, much after the same manner as blood smears, and this material is fixed by heat, the same result is obtained, as far as the staining properties are concerned, as if formalin or alcohol is used.

Independently, however, of the question as to whether this material is the result of fixation or other processes, the fact remains that normal cells present an appearance which is constant, and that degenerating cells present a picture deviating from this. It is not the idea of the writer of this paper to consider the usual forms of degeneration of ganglion cells, but to call attention to certain irregular types of degeneration not commonly met with.

If the nervous material is taken from the body within twelve hours and hardened in 96 per cent. alcohol, and then stained by the Nissl method, a picture is presented of a circular nucleus, vesicular, in a central position in the cell, and surrounding this arranged in regular order are seen the chromophilic bodies. When the cell undergoes degeneration, the cell protoplasm may take a deeper stain, the so-called pyknosis, with an arrangement of the chromatin in clumps, and clumping especially around the nuclear wall. The nucleus or more frequently the chromophilic elements either entirely or partially disappear, and the cell body stains with a light diffuse stain, giving the so-called diffuse chromatolysis (see Fig. 1). This is best seen in the effects of intoxication of different kinds on the nerve cells. The cells in this form may present a perinuclear diffusion of the chromatin, with the chromophilic elements intact at the periphery of

the cells, or the process may be complete throughout the cell. The cells in Fig. 1 present this form and are from a case of Landry's paralysis complicating pulmonary tuberculosis, at the Henry Phipps Institute. The nucleus in a degenerating cell becomes irregular in outline, loses its chromatin reticulum and finally disappears. During this process it "wanders" from its central position and takes a peripheral position at the edge of the cell body.

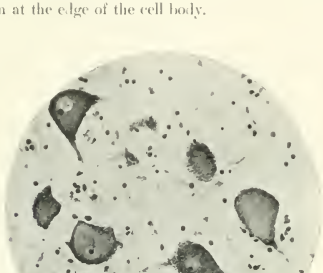

Fig. 1.—Diffuse chromatolysis. In cell in upper section of the picture, the nucleolus is seen outside the nucleus.

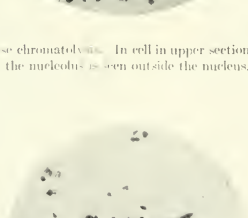

Fig. 3.—Ganglion cell showing ballooning and reticulum.

DEGENERATION OF GANGLION CELLS IN ADVANCED ARTERIOSCLEROSIS ESPECIALLY WITH REGARD TO CHANGES IN THE NUCLEUS.

In a cervical and lumbar enlargement of a cord of a case of rheumatoid arthritis with extensive cerebrospinal arteriosclerosis, the ganglion cells of the anterior horns were diminished in number, and the seat of the following changes: The yellow pigment occupied a large part of the cell area with an eccentric position of the nucleus and diminution in number of dendrites. The nuclei of most of the cells were of much smaller size and stained very deeply with the nuclear stain. The nucleus with the hemalaun eosin took a pale-violet stain, in which the filaments of chromatin could be seen under a high power. In the cells under consideration (see Fig. 2)

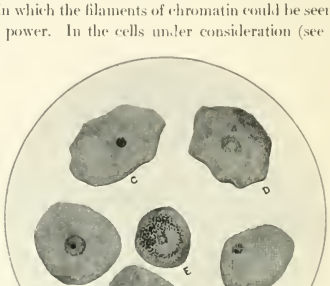

Fig. 2.—Cell changes in the spinal ganglia in a case of rheumatoid arthritis, with advanced arteriosclerosis. A, normal cell; B and C, diminution in size of nucleus; D, shadow nucleus; E, arrangement of pigment in Marchi stain. All stains except E stained by carbol hemalaun.

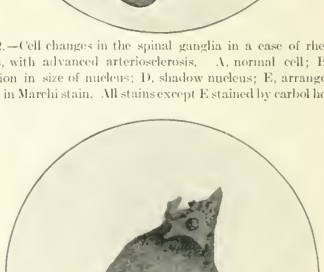

Fig. 4.—Ganglion cell from case of idiocy reported with Dr. Spiller.

the nucleus was reduced to one-half or even one-third of the normal size, took a deep-purple stain, in the midst of which the nucleolus was hardly perceptible. In a few of the cells the nuclear area was so reduced as to form a very slight ring around the nucleolus. The other ganglion cells, both in the cervical and lumbar enlargements, were fewer in number than in normal cords.

The normal ganglion cells should be spherical with a large vesicular nucleus, staining a very pale violet with hemalaun, with the cell substance staining a light purple. The chromophilic bodies of Nissl were distinctly stained and were in these cells finely granular and absent at the periphery of the normal cells. In the ganglia of this case it is the exception to find a cell approaching the normal. The yellow pigment described was present in these cells in large quantities. In some of the cells it appeared as a dark-yellow, homogeneous mass, whereas in others it occurred as very fine granules, giving a pale-yellow tinge to the cell protoplasm. The arrangement of the pigment in the spinal ganglion cells was somewhat different from that observed in the cells of the spinal column.

The usual arrangement of the pigment in the spinal cells is toward one end of the cell. In the spinal ganglia the deposition of pigment as a rule is around the nucleus in the centre of the cell. This is brought out very distinctly in sections by the Marchi method. The granular pigment in this case, both in the cells of the spinal cord and of the spinal ganglia, gave a black stain by the Marchi method, and a purplish black stain by the Weigert sheath stain. The same character of pigmentation with more advanced changes in the nuclei and other evidence of senile degeneration of the cells, both of the spinal cord and intervertebral ganglia, and the Gasserian ganglion, were present in a case of migraine with extensive arteriosclerosis of the central nervous system. In some of the cells, instead of a deeply stained, contracted nucleus, the

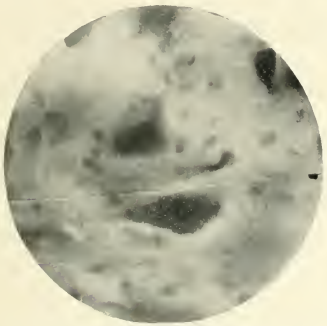

Fig. 5.—Photograph of ganglion cells, showing early stage of iron infiltration. Iron-hematoxylin stain.

Fig. 6.—Ganglion cells, showing advanced stage of iron infiltration, with degeneration of ganglion cells. Iron-hematoxylin stain.

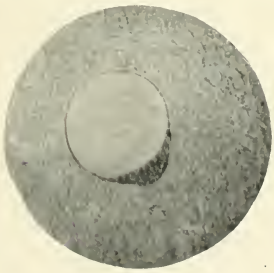

Fig. 7.—Vacuole formation in ganglion cell of anterior horn of spinal cord in a case of tuberculous meningitis.

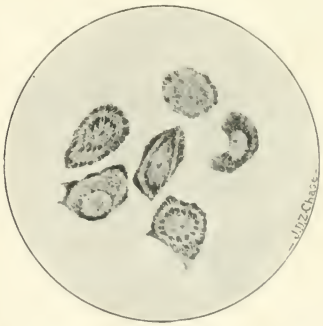

Fig. 8.—Ganglion cells from the suprarenal gland of a chicken. Stained by Nissl method. (Zeiss, oc. 2, ob. 3 mm.)

nuclei were very pale, without nucleoli and without the chromatin filaments of the normal nucleus. The chromophilic elements of the cell protoplasm stained less intensely in these cells, especially toward the periphery of the cell. The outline was somewhat irregular in shape. In more advanced stages of degeneration the cell outline is very irregular, the cell protoplasm taking a homogeneous pale-violet stain with a deposition of large quantities of yellow pigment at one side and sometimes taking up the entire cell area; the nucleus is either entirely absent or if present has an eccentric position at the edge of the cell and at time appears as a vacuolar area in the midst of a mass of pigment, but taking no stain and appearing as a clear, stainless area.

All these cell changes have been noted as occurring in the intervertebral spinal ganglia, and are also present in the Gasserian ganglion.

ABIOTROPHY.

Gowers has used the term abiotrophy to designate an inherent defective vitality of tissues manifested by loss of tone and vitality and degeneration after a certain period. This is manifested most distinctly in the muscular dystrophies in which the condition is dependent upon lack of vital tone of the muscles.

The same term can be used in another sense to apply to certain changes in the nerve cells. The problem that often confronts us in dealing with both conditions of nerve cells is to determine whether the changes are inherent in the development of the cell or acquired after the cell has reached its full development.

The study of the nerve cells in defective development of the nervous system gives us a picture distinctly different from that seen in the usual degenerative changes. Different grades of these changes may be seen.

In the case of a man of full cerebral development, but with a defectively grown spinal cord, occurring in the service of Dr. C. W. Burr, and reported by him, these changes were present. In this case a man of forty-three had a fully developed and normal-shaped head, with fairly normal intelligence, but with the body of a child of four or five years of age. The gross examination of the brain and spinal cord showed a fully developed brain, but with a spinal cord smaller than normal. The spinal ganglia is of normal size and appeared to be larger than normal on account of the small size of the cord. The anterior-horn cells in this case were normal in number and arrangement. The microscopic examination by the Nissl method gives the following changes: Cells appear tumefied and of an irregular balloon shape (see Fig. 3); the nucleus and chromophilic elements were heaped at one end of the cell corresponding to the apex of the balloon; the rest of the cell area was filled with a light-yellow material throughout which a dark reticulum could be easily discerned.

In a case of idiocy, in a girl of six, reported by Dr. Wm. G. Spiller and the author, the same type of cell degeneration or defective development, but to an extreme degree, was present (see Fig. 4). The changes in the nerve cells in these cases gave the same extremely tumefied, balloon-shaped appearance with the chromatin at one end of the cell. That this condition of the nerve cell was not due to hemorrhagic pachymeningitis was shown by the presence of the same changes in the basal ganglia, pons, medulla, and spinal cord. In another case of idiocy, which presented in its formation the symptoms of cerebrospinal meningitis, but in which there were no meningeal changes at autopsy, the same changes were found by Spiller. Hirsch and Sachs found the same changes in amaurotic family idiocy. While Hirsch considered these changes in amaurotic idiocy to be of toxic origin, Sachs holds that a disease so widespread as this, beginning always at the same period of life and attacking several members of the same family, with the exemption of others, could not be due to a toxic influence.

The presence of these cell changes, which have been found only in cases of idiocy or defective development, leads me to agree with Sachs that they are not of toxic origin, but are examples of defective development of the ganglion cells. This is confirmed by the presence of these cells only in the spinal cord in the case here reported, with normal-cell structure throughout the brain, which presented, neither during life nor autopsy, evidence of defective development.

A study of the ganglion cells of the adrenal gland in fowls presents a type of retrogressive abiotrophy. Embryologically the adrenal gland is developed in part from the Wolfian duct and in part from a branching off of the spinal ganglia. Distinct ganglion cells are observed as such as an essential element of the adrenal structure, no higher in the animal kingdom than fowls. A study of these cells gives the following characteristics: When a basic nuclear stain is used the nucleus presents marked changes. In some of the cells it is very pale; in some it is much darker than normal. The shape of the nucleus is very variable. In practically none of the cells examined was there a perfectly spherical nucleus. From a slight irregularity to a very marked lance-shaped nucleus, all varieties were observed. The nucleus is often peripheral in position. No normal nucleoli can be observed. Many of the cells have multiple nucleoli. In the majority of the cells what appears to be a distinct nucleolus is so irregular in shape as to constitute merely a massing of chromatin in the nuclear reticulum. The arrangement of this material is as irregular as the nuclear arrangement of polymorphous polynuclear leukocytes, and very often the nucleus has the appearance of such a stained leukocyte. In the body of the cell the chromatin is arranged in two distinct layers; one immediately surrounding the nucleus and the other at the periphery of the cell with a comparatively chromatin-free area between.

The cells are of more irregular shape than that of normal ganglion cells (see Fig. 8).

METABOLIC DEGENERATION OF THE NERVE CELLS WITH IRON INFILTRATION.

In early life, even antenatal life, the function of the ganglion cell is not definitely determined, and while irritability and other nerve functions are predominant characteristics of such cells, they may take on the other functions of cells in general. This is manifested when free blood is extravasated in the neighborhood of developing ganglion cells. This to a certain extent is true of fully developed ganglion cells, but not to the same degree. The ganglion cells, under these circumstances, take on an absorptive and metabolic function, as manifested by the presence of hemosiderin and other blood products within the nerve cells. When this condition takes place in the full-grown cell it is associated with degenerative and atrophic changes (see Fig. 6). In the developing cell, however, it gives rise to certain microchemical reactions, but with little chromophilic change in the cell outline (see Fig. 5). This condition may be seen both in the lower animals and in the human beings. In the case of a newborn puppy with deformities in the posterior extremities, sclerotic and hemorrhage foci were found in the lumbar enlargement, antenatal in their development. The microchemical and microscopic changes in these cells were as follows: When sections are stained by the Weigert or iron-hematoxylin stains, both of which stain the red blood corpuscles a deep black, the following changes in the neighborhood of the hemorrhage are seen: In the cells, at a distance from the hemorrhage, the nucleoli alone takes a black stain. This is true of nucleoli in general. As we approach the area of hemorrhage the cells become smaller and the nucleus becomes irregular and takes a jet-black stain. The rest of the cell body takes a very pale brown in which the chromophilic elements may be seen by careful inspection. In the next stage of iron infiltration the protoplasm of the cell body becomes darker; this is followed by granules of jet-black pigment, and in the area usually occupied by chromophilic elements. As this condition advances these areas are connected by fine filaments of jet-black pigment giving a reticular appearance to the cell protoplasm. In more advanced cases the clear areas in the cell are encroached upon by the pigment masses until the whole cell area, including the processes, present a jet-black appearance and the nucleus is no longer distinguishable. The nucleus is usually found in a central position, although it may occupy a very eccentric position. The neuroglia cells in the neighborhood of the above cells do not present the same change. They are somewhat darker and may contain a few jet-black granules, but are not completely infiltrated.

Van Giesen. The normal ganglion cell by the Van Giesen method presents the following picture: The cell body takes a deep-red stain in which can be seen the chromophilic elements. The nucleus has a vesicular appearance and is also red in color. It has a nucleolus of slightly darker tint. In the cells affected by the iron infiltration the cell body and the nucleus take a deep-yellow stain. The nucleoli cannot be seen in the deeply yellow-staining nucleus.

Hematoxylin Eosin. In the normal ganglion cells the slight pink tint of the cell body is in striking contrast to the nucleus, which has a vesicular appearance and takes a violet stain, as does also the nucleolus. The cell showing hemoglobin infiltration takes a deep-red stain and the depth of the stain increasing with the degree of pigmentation. The nucleus takes a deeper stain of red than does the cell body. The nucleolus cannot be seen. The position of the nucleus of some of the cells is eccentric.

As will be seen from these staining reactions, the cells take on the reactions for hemoglobin, and while, on account of the material in this case having been used for serial sections, the hemosiderin reaction could not be used, it has been found in other cases giving identical changes by Weber and myself. In a case of iron infiltration in the neighborhood of a hemorrhagic foci in the cortex of an adult, not only were the above changes found but also the hemosiderin reaction by the ferrocyanide-hydrochloric acid test. Weber, in his case, found identical changes.

It is not probable that a cell, whose function has been so disturbed during its developmental period, will develop to the same degree as the cell whose function has not been interrupted. Results, therefore, of traumatism and slight meningeal hemorrhage in the developmental period must be considered in other relations than that of simple traumatic pressure on nervous tissues.

These changes, to a lesser degree, are seen in cases of acute destruction such as rattlesnake poisoning, etc.

In Fig. 7 an extreme grade of vacuolization of the nerve cell is pictured. The chromophilic elements are massed at one end of the cell, with a few elements around the wall of the vacuole. There was no evidence of postmortem change in this case.

GANGLION IN THE FLEXURE OF THE ELBOW.

By Astley Paston Cooper Ashhurst, M.D.,
Surgeon to the Out-patient Department of the Episcopal Hospital; Prosector to the Associate Professor of Applied Anatomy in the University of Pennsylvania.

George B., aged fifty years, applied February 1, 1907, to the Out-patient Department of the Episcopal Hospital for loss of power of his hands. On examining the arms it was found that in the bend of the left elbow there was a cystic swelling, the size of an egg, not tender, not inflammatory, with neither pulsation nor bruit, which became very tense when the elbow was fully extended (Fig. 1), and became less tense and presented indistinct fluctuation when the elbow was flexed. The patient stated that he had discovered it accidentally one morning about two months before. The numbness and loss of power, which affected both hands equally, had commenced several months before this swelling made its appearance, and the two appeared to have no rela-

Fig. 1. Ganglion in flexure of left elbow. Forearm in full supination and viewed from ulnar side.

tion to each other. The swelling in the elbow could easily be moved laterally beneath the skin, but its longitudinal mobility was limited. It overlay the brachial artery, but evidently had no connection with it. The radial pulse was normal.

The cyst was considered to be a ganglion of the tendon of insertion of the biceps muscle, or possibly a ganglion connecting with the elbow-joint. The patient said the swelling did not trouble him, and he desired no treatment for it. He was therefore referred to the medical dispensary.

The patient later returned and requested that the tumor be removed. This was done under cocaine anesthesia on March 16. The ganglion was found to be densely adherent to the tendon of the biceps, and to have its pedicle attached to the tuberosity of the radius beneath this tendon. The cyst had made its way to the surface on the outer side of the biceps tendon, but had not broken through the deep fascia, which was carefully dissected off the cyst. Its contents were clear serum. After excision the ganglion was stuffed with cotton, the attachment of the pedicle sutured, and a photograph made (Fig. 2).

The bend of the elbow appears to be one of the rarest situations in which a ganglion may develop. Very frequent on the extensor surface of the wrist, they are not unusual on its flexor surface and on the anterior surface of the ankle. Ganglia in the popliteal space are rare, though by no means unknown; two such cases have come under my own notice within the last few years.

A somewhat extended search has revealed the following reports of ganglia in the flexure of the elbow:

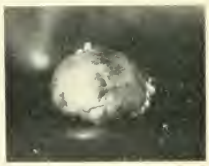

Fig. 2.

1. Agnew recorded the case of an adult female, in the bend of whose left elbow there was an elastic, sensitive tumor the size of a hickory nut, on the inner side of the tendon of the biceps. Its duration had been two years. By pressure on the median and posterior interosseous nerves it had caused paresis of the forearm muscles. Extirpation was undertaken, and the tumor was found to be connected by a pedicle with the bursa between the tendon of the biceps and the tubercle of the radius. The tumor had become solidified by the formation of fibrous tissue.

2. Hyrtl describes a ganglion in the bend of the elbow which during life was diagnosticated as an exostosis because it was so tense.

3. Dubrovo reported a case of "hygroma proliferum sarcomatodes profundum" affecting the flexure of the elbow. This reference I have only from the *Index Catalogue* of the Library of the Surgeon-general's Office, and have not consulted the original.

4. Rieffel reported the case of a man, aged forty-one years, who complained of feebleness of the right forearm, of inability to flex the elbow completely, and especially of loss of complete pronation of the forearm. When the elbow was partially flexed there could be felt a swelling, the size of a small walnut, resistant, non-pulsatile, and tender; when the elbow was fully extended the tumor could not easily be distinguished It was situated on the outer side of the biceps tendon and was not movable transversely or longitudinally. It had developed suddenly, during the act of whipping a horse. It was evidently not inflammatory. Extirpation under cocaine was undertaken: the tumor proved to be a hematoma of the bicipital bursa, undergoing cystic transformation. The operation was followed by perfect recovery of function.

Rieffel says that Schwartz had told him of a similar case which had been under his care, but of which he had no notes. In the discussion which followed the reading of Rieffel's paper, Mignon and Ricard each mentioned a case which they thought analogous. As far as can be told from the printed report of Mignon's case, it does not seem to me that it should be included here.

Vogt is one of the few systematic writers to treat of affections of the tendon of the biceps. He merely mentions them in passing, referring to the case recorded by Hyrtl. Nancrede gives a somewhat more complete account, quoting Agnew's case. Later systems do not even mention the condition.

The chief interest centres in the diagnosis. The ganglion might be mistaken for an aneurysm, an abscess, a fatty tumor, a sebaceous cyst, or, as in Hyrtl's case, for an exostosis. The first is readily excluded by the absence of all arterial signs, or by the absence of expansile pulsation should pulsation of any kind be transmitted from the brachial artery. Abscess may be excluded by the duration and general characteristics of the swelling. A lipoma would not be so distinctly cystic, nor would it become so tense when the elbow was extended. The free mobility of the skin over the swelling serves to distinguish it from a sebaceous cyst. A cold abscess in the elbow-joint will scarcely ever point anteriorly; but apart from this fact, the history of the patient will be sufficient to exclude all joint trouble of a tuberculous nature. Rieffel's case explains the pathology of the condition in a very satisfactory way.

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PRIMARY CANCER OF THE GALL-BLADDER: WITH REPORT OF FOUR CASES.[1]

By Lucius W. Johnson,
Class of 1907.

(From Pathological Laboratory of University of Pennsylvania.)

The interest of the writer was directed to the subject of primary cancer of the gall-bladder from the study of 4 cases herein detailed, for which material he would here express his thanks to Dr. Allen J. Smith, and Dr. George P. Müller. The general subject seems of sufficient importance and general interest to warrant a statement of the conclusions arrived at from a study of the cases recorded in the literature, available to the writer, and at the same time a description of the cases in the writer's possession.

Cancers of the gall-bladder are not infrequent; some are the result of secondary invasion, but the greater number are primary to the wall of the gall-bladder itself. From the available literature 33 cases of undoubted primary occurrence have been collected, to which are added the 4 cases in the author's possession; forming a group of 37 cases for study.

Classification. From the published descriptions of some of the cases it is impossible to be convinced of their type; but it is possible to roughly classify them as being in 28 cases scirrhus, in 4 medullary, and in 1 colloid. Of the rare but well-recognized, flat-cell, or squamous epitheliomas of the gall-bladder no instance is included in this group; but the author has had the opportunity of seeing such a specimen which has been studied by Dr. John Speese and recently reported by him before the Philadelphia Pathological Society. This specimen shows clear evidence of the squamous nature of its cells, many exhibiting well-marked prickle borders and often being arranged in well-formed, pearly bodies.

The division of these cancers, from a histological standpoint, excluding for the time the rare squamous epitheliomas, into adenocarcinoma and carcinoma simplex, is of little moment, and, from the meagreness of many of the descriptions, is impossible.

[1] Read before the Philadelphia Pathological Society, March 25, 1907

Theoretically, it should be possible to divide the various examples, from the source of their original cells, recognizing those springing from the lining cylindrical cell layer of the organ and those arising from the cells of the mucous glands of the mucous membrane, or, possibly, from aberrant epithelial structures in the wall. Thus, we might expect to find varieties in which an ordinary infiltrating cylindrical cell epithelioma with little or no attempt at gland formation would be formed from cells of the lining mucous membrane; or examples of a lenocarcinomatous types, perhaps with mucin formation ("colloid" adenocarcinoma), developing from the cells of the mucous glands. So, too, it might be suggested that in the event of a growth of purely superficial origin there might be a greater likelihood of a definite medullary type being found than in growths originating deep in the wall from the mucous glands, where a more active stroma formation might lead to a scirrhus form. Such reasoning, though theoretically warranted, is not justified by the material in hand and so is pursued no further.

Etiology. Analysis of the material collected shows that an important relationship exists between cancers of the gall-bladder and gallstones, cholelithiasis existing in all but one of the group of cases studied. Various authors estimate gallstones to be present in 85 to 96 per cent. of primary gall-bladder cancers. The action of gallstones as sources of irritation, leading in time to inflammatory changes of structure and cell proliferation, is an important one and may, with reason, be generally conceded; yet there is reason, as shown in one of the original cases of this paper (Case I), to believe that gallstone formation may at times be a result rather than a predecessor of the neoplasm. In seeking a reasonable explanation of the causal relation of gallstones probably the most important factor to be thought of is the inflammation which is either induced by the stones or underlies the calculus formation. While not universally accepted as correct, Ribbert's suggestions may be considered as throwing some light on this feature. All cancers may be looked upon as growths of epithelium displaced in their relations to their surroundings and developing into independent epithelial formations. Ribbert has suggested that in chronic inflammations characterized by connective tissue formation the new fibrous tissue may gradually penetrate basement membranes, growing between the cells of a surface or a gland so as to separate a cell or a group of cells without materially interfering with its vitality or nutritional supply; such a cell or group of cells in continued proliferation being the basis of the cancerous formation. Such isolations may frequently occur in wound healing and even in ordinary inflammation; nevertheless, only a small proportion can be believed to actually develop into cancers. Only now and again, Ribbert argues, can all of the essential conditions for successful proliferation obtain; probably the vast majority of such cell isolations are, by the pressure of the sclerosed tissue or by nutritional changes produced by the sclerosis, doomed to elimination by pressure atrophy, starvation, or degeneration. Moreover, in isolations in acute inflammations the alterations in the cells produced by either the cause of the inflammation or by rapid change of nutritional supply leave little chance of sufficient vital energy being retained for continued proliferation; hence, the relationship with the slower, more gradual, and less toxic chronic inflammation appears more favorable for the origin of cancerous foci.

Reasoning along such lines, a series of events leading up to the production of cancer in the gall-bladder may be imagined; as a beginning we may have a cholelithiasis, which may be thought of as a mechanical source of continual irritation; or we may have an altered character of the contents of the gall-bladder dependent on infection of the bile, which is known to be not infrequent, acting as a special irritant; or we may have the gall-bladder involved in an extension of inflammation from a neighboring structure. All or any of these conditions may induce a chronic inflammation of greater or minor degree of severity, with gradual sclerotic changes, in the course of which isolations such as Ribbert mentions may be accomplished either from the glands in the mucous membrane or from the lining itself.

Aside from the influences mentioned above as potential causes of chronic inflammation we should think also of the pressure by tight lacing. Not infrequently the effect of lacing is seen upon the surface of the right lobe of the liver as a fibrous and atrophic area with marked thickening of the capsule; this sclerotic capsulitis may be seen extending to the border of the liver in the region of the gall-bladder, producing adhesions to the latter and quite possibly a process of induration of its wall. In this connection it is of interest to mention a case reported by de Saint Fusciens:

The subject was a shoemaker, who, in the pursuit of his trade, was accustomed to press his shoe-vise against the abdomen. An area of peritonitis with adhesions to the gall-bladder was found beneath the area of pressure and in the wall of the gall-bladder at the point of adhesion a cancer had developed. The sequence of events seems clear and regular if we accept the view of cancer production from inflammation.

Heredity as a basis can be traced in so few cases as to be practically negligible; though 2 of the original cases here reported had a family history of malignancy.

The distribution of primary gall-bladder cancer according to age parallels that of cancer in general. de Saint Fusciens gives the following table with which analysis of the 37 cases studied is compared:

	De Saint Friscien. Per cent.	37 cases. Per cent.
30 to 40 years	9	4
40 to 50 "	19	20
50 to 60 "	27	24
60 to 70 "	19	32
70 to 80 "	14	20

Arrangement of Cases by Sex shows an interesting relation, various authors finding from 80 to 95 per cent. of cases (72 per cent. of this series) occurring in females. It is a striking fact that the proportion of gallstone cases occurring in women is very close to that of gall-bladder cancers in that sex, strongly suggesting an interdependence or a common cause; this frequency may be due to the sedentary habits of the sex, the pressure of corsets and tight lacing, or the mechanical disturbances of the abdominal viscera during pregnancy, these possibly giving rise to portal circulatory faults which predispose to chronic cholecystitis or to the deposition of bile salts as calculi, and thus to cancer formation.

The relationship of cholelithiasis to cancer should not be passed by without mentioning cases in which appearances suggest that the cancer precedes the calculus formation, the gallstones presumably depending on the cancer or the accompanying inflammation for their production. It is possible that both the cancer and the associated inflammation may provide a nidus for determining the precipitation of the cholesterin and bile pigment for the growth of the calculus. One of the appended original cases (Case I) is clearly in line with this thought, showing on the early cancerous mucous membrane a deposit of cholesterin and a collection of the same material in a small, isolated, cancerous pocket in the depth of the wall. We are not justified, however, in concluding, as have Morin, Vansant, and others, that all of the gallstones are secondary formations, or that the cancer-gallstone sequence even occurs frequently; primary cholelithiasis with subsequent cancer formation must be regarded as the course of events in the very great majority of cases.

Point of Cancerous Origin in the Gall-bladder. Of the cases under consideration in which the primary seat could be determined, 7 originated at the neck of the bladder, 7 at the tip, and 1 at that part of the upper wall in contact with the liver. Ames found, in 12 cases, 6 at the neck and 6 at the fundus. The selection of the primary site may be explained by the movements of the gallstones in cases of preceding cholelithiasis; the stone being carried toward the opening of the duct by the current of outflowing bile, stopped here by the narrowing of the lumen and falling back to be caught again in the current flowing toward the outlet; each such movement produces a mild trauma which, repeated often enough, may lead to chronic inflammation and cancer formation. An analogous explanation might account for the cases arising from the fundus, the stones collecting here by gravity and being moved about by the muscular contractions of the wall. The case in which the primary seat of the cancer was in the upper wall in contact with the liver showed this point to be also the position of adhesions to the liver, apparently an extension of an hepatic capsulitis from the convexity of the liver.

As to the precise type of cells, which in various cases give origin to the cancerous growth, little of value can be stated other than that the majority of instances show columnar cells of the character of the lining cells of the viscus as their prevailing type, and that in a certain proportion the more mucus character of the cells and their greater tendency to acinous formation suggest that they arise from the elements of the small mucous glands in the mucosa. Weber and Gottschalk have discussed at length the possibility of metaplasia of the columnar cells of the mucosa into a horny pavement type on surfaces exposed to trauma by gallstones, especially upon the surface of a growing cancer; while the metaplastic idea is by no means a satisfying one, we know of no more acceptable surmise as to the origin of the flat cells of such growths. Gottschalk has described a case in which the cancer cell resembled the liver cells in that they were polygonal, had large nuclei, granular protoplasm, and frequently contained fat droplets; this suggests the possibility of metaplasia or of origin from hepatic cell rests, either of which are subjects too large for discussion here.

Character of Growth and Extension. The scirrhus cancers in this situation are characteristically marked, as described by Morin, by immense thickening of the wall and ulceration of the cancer surface with induration. The medullary forms generally show a fungoid thickening protruding into the cavity of the bladder, soft and vascular in type. As a rule this form has a relatively small bladder lesion with early and marked extension along the gall-ducts into the liver; jaundice is said to occur early, due to obstruction. The scirrhus variety as a rule involves the gall-bladder wall in a wider area with great thickening and induration and contraction of the lumen; it does not characteristically show as widespread metastasis, but is apt to form adhesions to the liver and may invade through such adhesions; jaundice is said to occur late in this type.

In 25 of the cases studied, the existence and site of metastasis is noted. In 20 of these the liver is named as the sole site of the metastasis or as one of the multiple sites; in 8 the peritoneum is stated to have been involved; the pancreas in 3; the wall of the stomach (not merely its peritoneal covering) in 2; the duodenum in 1; the spleen in 1; the left kidney in 1; one or both ovaries in 2; the diaphragm in 2; the pleura in 2; the lungs in 1; the abdominal wall at the navel in 1; definite lymphatic involvement is mentioned in only 5, but this is probably because only very widespread involvement is mentioned; the statement of extension by the walls of the ducts and along the portal vein is made in several of the cases and

probably these should be added to the group of extension by lymphatics. It seems probable that of all the modes of extension, lymphatic distribution is most common.

Bearing upon the above and forming a part of the group upon which the conclusions were founded, the following 4 original cases are presented:

Case I.—M. W., female, aged forty-five years, weight 310 pounds. Family history negative except that maternal aunt died of cancer of breast. Patient has had three children, no miscarriages. No mention in history of any symptoms referable to gall-bladder disease.

Autopsy. Gall-bladder large, adherent to omentum by tip, full of thin, yellowish bile; cystic duct impacted by gallstones, one stone measured 2.5 x 3 cm. The wall was thickened and ribbed; at tip is a roughened area covered by a yellowish, plastery deposit of cholesterin; here the wall is double, the enclosed space being lined with a smooth membrane and filled with cholesterin in a soft, granular deposit.

Microscopically (tissue from thickened area with double wall). The general structure is made up of loose connective tissue; a certain area shows nearly normal structure; adjoining this is an area in which the cells of the lining membrane are greatly multiplied, vary considerably in size, and are irregularly arranged, having broken through the basement membrane. Sections which include the pocket filled with cholesterin mentioned above show a similar cancerous structure. A small lymph node in this part of the wall shows enlarged follicles, but no cancerous invasion. Scattered through the mass are several oval or round cells with large protoplasmic masses and 15 to 25 nuclei; these bear a close resemblance to syncitia, but are probably due to rapidity of growth, the nuclei having divided more rapidly than the protoplasm.

The cells in general are of well-marked columnar type, corresponding more closely to the cells of the lining mucous membrane than to those of the gland. In their new situation the misplaced cells have evidently continued their function of cholesterin elaboration, as shown by the cholesterin found in the pocket. Probably, on account of the marked sclerosis from chronic inflammation, the wall has been too dense for rapid extension, there being no secondary involvement.

Case II.—This specimen was found in the collection of the Laboratory of Surgical Pathology. Of its history nothing is known; it having been kept for some time as a specimen of hydrops of the gall-bladder.

Microscopically. The section shows the wall markedly thickened and the mucous membrane destroyed; the inner portion is thickly infiltrated with polynuclear leukocytes; the deeper portions are sclerotic and edematous and less markedly infiltrated with leukocytes. The cancer is mainly in the inner part of the wall and consists of interlacing cords of cells extending in many planes; the cells are irregular and polyhedral, many are degenerated and much of the cancer shows necrotic change; leukocytes are frequently found between the cancer cells. From the appearance of the cells the classification would be a scirrhus carcinoma simplex; suppuration is also present.

Case III.—Female, aged fifty-six years. Family history negative.

Autopsy record stated that a large cancerous mass was found originating in the gall-bladder and involving liver, peritoneum, and diaphragm. No statement as to gallstones.

Section shows peritoneal structure much thickened, much fibrous tissue with embryonic elements showing mitotic figures; the cancerous invasion spreads through as a carcinoma simplex with little definite arrangement, the cells for the most part being in solid masses. Many cells are of seal-ring type, distended with mucin and some showing the finely granular or reticular appearance of the mucin. Many cells show large hyperchromatic nuclei. By means of adhesions it has extended to the border of the liver, giving massive involvement of that organ, and beyond the mass are isolated, capsulated, metastatic masses. In one of the vessels of the wall is a thrombus containing cancer cells and a widespread perivascular round-cell infiltrate which suggests that the dissemination may have been vascular in part.

Case IV.—C. K., male, aged thirty-nine years. Mother died of disease of liver, with gallstones.

Patient had typical attacks of Charcot's fever for eighteen months before operation.

Operation. Cholecystectomy; gall-bladder was found shrunken and adherent to the liver; it contained several gallstones.

Microscopically. Section shows part of mucus and muscular layers of gall-bladder wall and a few shreds of the serous portion. Some of the glands extending in from the mucous surface are quite normal, with an intact basement membrane; others show a broken membrane with proliferation of the lining cells. The muscular fibers are separated by groups of round or columnar cells and some young connective-tissue elements. The cancer does not extend deeply into the tissue; the superficial part is necrotic and ulcerated, the surrounding tissue congested and edematous. The cells resemble somewhat those of the lining membrane, but the arrangment closely follows that of the glands; probably an adenocarcinoma.

Like Case I the lesion is very early in development and there is no evidence that any secondary growth took place.

In conclusion the author would acknowledge his obligations to Dr. Allen J. Smith and Mr. Henry Hutchinson for assistance in collection and arrangement of data.

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BOOK REVIEWS.

Pulmonary Tuberculosis. Its Modern and Specialized Treatment. By Albert Philip Francine, A.M., M.D. Pp. 247. Philadelphia and London: J. B. Lippincott Co.

The volume before us, as might naturally be supposed, is one of a considerable number of publications, which have appeared in the past two or three years, upon such an important and engrossing a subject as that of Tuberculosis. Many have been larger in size and in scope, and some have been smaller, but we believe the author has struck a very happy medium, in the present treatise dealing only, as he professes, in the modern and specialized treatment of the disease.

In the volume before us exhaustive advice is given along the lines of prophylaxis, attention to which is so necessary, if the beginning hopeful signs of reducing and perhaps eventually stamping out this fearful malady are to point truthfully to a successful ending. Care of the nasopharynx, not only to prevent recurrence, but to prevent occurrence of hemorrhage, is strongly urged, and so prevent the harboring of the pathogenic bacteria of mixed infection, to whose presence the hemorrhage is due. In pulmonary tuberculosis, owing to the constant opportunity for infection of the gastro-intestinal tract by swallowing the secretions not expectorated, we believe there is much more frequently organic involvement of this tract than the author admits, and that careful treatment here is of prime importance, especially as there is such a demand for increased nourishment from this tract.

In discussing the treatment for hemorrhage, after giving absolute rest and the application of ice locally, as the best means for combating this dangerous accident, mention is made of the use of nitroglycerin in those cases due to circulatory hypertension, always, at such times, watching the case closely, until the high blood pressure is overcome.

In those cases not due to high blood pressure the use of adrenalin chloride, and of the other derivatives of the suprarenal bodies, is recommended. Owing to the sclerotic effects which this drug has been shown to produce, with the subsequent formation of brittle spleens, pipe-stem arteries, and even aneurysms, we believe its use for other than purposes of emergency, or over more than very short periods of time, should be very guarded.

The chapters on Tuberculin and Serum Therapy deal in a thorough and comprehensive way with Koch's and Beraneck's preparations of tuberculin and with von Behring's kindred discovery and with Maragliano's, Marmorek's, and the antistreptococcic sera.

Throughout, we cannot but feel impressed by the sound advice which permeates the entire work. The necessity for rest, fresh air, and nourishment above all else, is urged and repeated, time and again, whether for cough, hemorrhage, fever, or what not, and so we believe we may recommend, most honestly, this work, especially to the general practitioner, as presenting exactly that sound teaching which will redound to the most benefit, both to his patients and to himself.

H. K. H.

STOHR'S TEXT-BOOK OF HISTOLOGY. By DR. FREDERIC T. LEWIS, Assistant Professor of Embryology at the Harvard Medical School. Sixth American from twelfth German edition, arranged upon an embryological basis. Philadelphia: P. Blakiston's Son & Co., 1906.

At first glance one has considerable difficulty in recognizing that this recent edition of *Stöhr's Text-book of Histology* has any relation to the preceding ones. Under the new editorship of Dr. Lewis there appear so many changes in form and matter, that quite a new character is given the book.

As mentioned on the title page, the chief departure is in the great amount of attention paid to the developmental stages of the tissues and organs. Not only is the adult form of these described, but also their principal embryonic phases. Many illustrations are added bearing on this part of the text; some other new ones drawn from various sources. By the treatment of histology from this standpoint we are given the entire life-history of the organs—their "developmental possibilities" as well as their mature form. The editor is in full sympathy with the revised anatomical nomenclature, but very wisely usually gives the older terms as well. In text-books, at least, it will be, no doubt, a long time before the name of Stenson is omitted in describing the parotid duct, or of Hassall in referring to the thymic corpuscles. But while the elimination of proper names is in the direction of simplification, one feels very doubtful if calling masses of lymphoid tissue lymph glands and grouping such "glands" with ovary and testis as cytogenic glands is an advance.

The text has been modernized throughout, but it is especially in the blood-vascular system that the editor incorporates results of new work. He follows Dr. James H. Wright in describing platelets as the broken-off pseudopodia of the giant cells of the bone-marrow, and with Weidenreich he figures the red blood corpuscles in the circulation as cup- or bell-shaped. The term sinusoids (a product of the Harvard School) is used in describing the portal-vein capillaries of the liver—the difference between true capillaries and sinusoids being wholly an embryological question, based on the manner of their first formation. In its changed form this book, while not so well adapted to the elementary student, will be a welcome addition to any histological laboratory.

W. H. F. A.

UNIVERSITY OF PENNSYLVANIA.

PENNSYLVANIA RAISES THE REQUIREMENTS FOR ADMISSION TO MEDICAL SCHOOL.

RECOGNIZING the advantages of a broader general education and the growing necessity of the prospective student having in addition special preparation for the study of medicine, the Board of Trustees of the University of Pennsylvania has decided recently to raise the requirements for admission to its medical school. These requirements include two years of general college training and in addition a certain knowledge of biology, chemistry, and physics. According to the plan which has been adopted, the standard will be raised gradually, beginning with the academic year 1908–1909 and reaching the maximum 1910–1911.

PATHOLOGICAL SOCIETY OF PHILADELPHIA.

NOTE.

The Pathological Society of Philadelphia, which is one of the oldest if not the oldest Society of its kind on this continent, will celebrate its Semi-centennial in May, 1907. Instituted at a time when pathology scarcely had a foothold in this country, it has kept pace with the tremendous development of that science, and has had a share, not only in giving Philadelphia its eminence as a medical centre, but also in fostering the scientific spirit in America.

The celebration, which may rightly be considered an event of national importance, will extend over two days: Friday, May 10th, and Saturday, May 11th. On the first day addresses will be delivered by Dr. Frederick G. Novy, of Ann Arbor, Michigan, on "The Role of Protozoa in Pathology;" by Dr. Simon Flexner, of the Rockefeller Institute, New York, on "The Newer Pathology;" and by Dr. A. E. Taylor, of the University of California, on "The Dynamic Point of View in Pathology."

In the afternoon, at 4 P.M., a commemorative meeting will be held in the Pennsylvania Hospital, where the first meetings of the Society, in 1857, took place. At this meeting Dr. William Osler, Regius Professor of Medicine, Oxford University, England, will deliver an address on "Pathology and Practice."

At a dinner in the evening, prominent men from all parts of the country will respond to toasts.

An exhibition meeting of interest to pathologists, clinicians, and surgeons will be held on Saturday, May 11th.

The date of the celebration will enable those to be present who have been in attendance upon the Congress in Washington, and those who are coming East a little in advance of the meeting of the American Medical Association.

UNIVERSITY OF PENNSYLVANIA
DEPARTMENT OF MEDICINE
FOUNDED IN 1765

This Medical School, the oldest in the United States, was founded in 1765 by Dr. John Morgan, who filled in it the first medical professorship created in America. In his opening "Discourse upon the Institution of Medical Schools in America," delivered in the College of Philadelphia May 30, 1765, Dr. Morgan uttered these prophetic words: "Perhaps this medical institution, the first of its kind in America, though small in its beginning, may receive a constant increase of strength, and annually exert new vigor. It may collect a number of young persons, of more than ordinary abilities, and so improve their knowledge as to spread its reputation to distant parts. By sending these abroad duly qualified, or by exciting an emulation amongst men of parts and literature, it may give birth to other useful institutions of a similar nature, or occasional rise, by its example, to numerous societies of different kinds, calculated to spread the light of knowledge through the whole American continent, wherever inhabited."

Through Dr. Morgan, the pupil of Hunter in London and of Cullen in Edinburgh, the graduates of this school take a just pride in regarding it as the lineal descendant of the best medical schools of Great Britain in the last century. To Dr. Morgan was soon joined another pupil of Cullen, Dr. William Shippen, as Professor of Anatomy and Surgery, thus forming another tie of relationship to the celebrated University of Edinburgh, whose methods of instruction were substantially adopted here. In the next year Dr. Adam Kuhn was added as Professor of Botany and Materia Medica; and in June, 1768, a "Commencement was held," at which medical honors were bestowed, the first in point of time in America. In 1769, Dr. Benjamin Rush was elected Professor of Chemistry, while Dr. Thomas Bond, one of the trustees of the College of Philadelphia, delivered lectures on Clinical Medicine in the Pennsylvania Hospital.

To the faculty thus composed of Morgan, Shippen, Bond, Kuhn, and Rush, have succeeded, at various times, professors whose reputation has been national, such as Wistar, Barton, Physick, Chapman, Hare, Gibson, Horner, Dewees, Jackson, George B. Wood, Hodge, James B. Rogers Carson, R. E. Rogers, Leidy, Henry H. Smith, Pepper, Francis Gurney Smith, Stillé, D. Hayes Agnew, Goodell, W. Pepper, Jr., and Ashhurst.

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Admission to the Department of Medicine may be obtained either: I., by diploma; or II., by examination; or in certain cases, as specified below under I., by a combination of both methods.

I. Admission by Diploma: Any candidate who may have received a degree in Arts or Science from a college recognized by this University will be admitted without examination. Candidates who may have been admitted by examination to the two-year course in Biology of this University, and who may have satisfactorily completed the course, will be exempt from the entrance examination. Any candidate who may present written evidence of having passed the entrance examinations of a recognized college, in which the requirements are equivalent to those demanded for entrance to the Freshman Class of the College (Arts and Science Courses) of this University, will be admitted without examination.

Diplomas of public high schools may be accepted as complete or partial certificates. All diplomas presented by candidates will be referred to Faculty Committee No. 1 of the College Faculty (Academic), who will examine each case and decide whether the diplomas shall be accepted in lieu of examinations, and what subjects they properly cover. The diploma must be transmitted to the Dean of the Medical Faculty not later than June 10 or September 10 in each year, and must be accompanied by a certificate signed by the principal of the school, stating the exact amount of each subject covered by the diploma, and the mark or grade attained in each subject.

II. Admission by Examination: The required subjects of examination for entrance to the Department of Medicine are the same as those prescribed for admission to the Freshman Class of the College (Arts and Science Courses) of the University of Pennsylvania.

The course of instruction extends over four years, with one session, beginning the last Friday in September and ending on the third Wednesday in June in each year.

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SOME OF THE RECENT IMPORTANT CONTRIBUTIONS TO OUR KNOWLEDGE OF HEART DISEASE.[1]

By C. N. B. Camac, M.D.,
New York City.

At the suggestion of the Dean of your Medical School I give this clinic, and in doing so I feel a peculiar pleasure as I have not been officially in these halls since I sat as an undergraduate on those benches. I say undergraduate rather than student, as I am still the latter and hope to be for many years to come.

A word regarding the Alumni meetings being held at this time. When you are alumni, come to these gatherings—230 Medical Alumni sat down to dinner a few nights ago. I assure you the seeing of one's old colleagues, and learning what they have done and are doing, is an influence both stimulating and broadening. Just as thing knowledge is the best exponent of book knowledge, so a knowledge of men is the best way to know one's self. The first few years of beginning practice it may be harmful to leave; a man had better be on hand, even though it be to catch that call that does not come; but a little later you can manage to get away for the Alumni meetings if you have your heart set on it. If you once begin to go you will go often. We must attend these meetings with the spirit which, in our profession above all others, we cannot begin too early to cultivate, that spirit which seeks rather to give than to get; come with the altruistic spirit, for our college needs its graduate sons in carrying on the great educational work.

As subject for this clinic, which, on account of the epidemic of diphtheria now prevalent in this hospital, must be a talk, I have taken some of the recent important additions to our knowledge of disease of the heart. Examinations, final and hospital, are in the minds of most of us just now and I will endeavor to give you some material, not yet in the text-book, by which your answers may be rounded out and added to, and in consequence perhaps "a little better" than the other fellow, which, in competitive examination, counts for something.

Advances have been made in the last few years in our knowledge of —

The cardiac muscle,
The cardiac nerves,
The cardiac valves.

[1] A clinic delivered to third and fourth year medical students of the University of Pennsylvania, February 23, 1907

Cardiac Muscles. The clinical index of the state of the heart muscle is—

The rate,
The rhythm,
The intensity.

These three commonly neglected in the clinical teaching of heart disease may be of first importance, if considered not *separately but together*. I will speak more especially of rate and rhythm.

These three cannot be sharply separated in considering the lesions of the cardiovascular system; probably in any disturbance of the circulation, either functional or organic, all take part. Certain it is, however, that great disturbance of the heart's action may occur without any disease of the heart muscle, valves, or ganglia existing. To be able to distinguish these clinically is of great moment in many instances. Profound organic destruction of the heart and vascular system may exist without presenting any of those classical pictures which we have learned. An individual may be going about in his usual manner of life without dyspnea and edema, and without cardiac murmurs, yet his heart be in its last day or week of vital power. By a careful study of the rate, rhythm and intensity *considered together*, sometimes, not always, an index of the condition may be had. These may also offer evidence of beginning organic disease. As with incipient pulmonary tuberculosis, the early detection of the disease allows us to institute hygienic and dietetic measures which may maintain the health of the individual for many years. We are yet much in the dark regarding the clinical significance of the many disturbances of rate and rhythm, and it must not be supposed that variations from the normal indicate in all cases disease of the heart. Upon some points, however, we have had light thrown lately. I will endeavor to present these.

The normal rhythm or cadence consists of a long sound, a short pause, a short sound, and a long pause. During the pauses the heart rests. The rest periods exactly equal the work periods, so that the heart works one-half of the cycle and rests the other half. Encroach upon these pauses by disturbed rhythm or rapid rate and the heart is *working overtime*.

Disturbance of rhythm falls into two large groups—

1. Allorhythmia—regular irregularity,
2. Arhythmia—no regularity.

There are two peculiarities of the heart muscle which must be remembered. The heart muscle contracts to its maximum or not at all in response to any stimulation—this is known as the property of "maximal contraction." The other peculiarity is that after a contraction the muscle passes through a period or phase in which no stimulus can produce a contraction until this period is passed—this is called the "refractory phase." This latter possibly safeguards the heart against fatigue which might result if the first of these properties alone was active.

Clinically there are many subdivisions of allorhythmia such as pulsus alternans, pulsus bigeminus, pulsus paradoxus, pulsus intermittens, etc. The common terms regarding rate are tachycardia and bradycardia. Most of these are but terms expressive of what is felt regarding the cadence of the beats and offers us no clinical distinctions. The following admirable summary of the physiological data, by Professor Barker, is helpful in considering this subject:

"Physiologists now believe (1) that rhythmical contraction is a power inherent in the well-nourished heart muscle itself; (2) that all parts of the heart muscle possess this automatic rhythmical power, though in varying degrees; (3) when isolated pieces of heart muscles from different portions of the myocardium are studied the number of contractions in unit time varies for the different parts, the rate being fastest in the sinus; (4) the sinus, by virtue of this quicker rate, transmitting the contraction impulse to the atria and ventricles, sets the pace for the heart and so obscures the natural rhythmical automatism of the other muscular parts; (5) the contraction wave passes through the heart from muscle cell to muscle cell, rather than by way of the nerve (Gaskell, Engelmann); (6) the rate of rhythm, the force of the contraction, and the rapidity of the conduction of the contraction wave are dependent, in the main, upon the condition of the heart muscle itself; this, in turn, depending upon (*a*) materials brought to it or taken from it; (*b*) work done by it; (*c*) nerve impulses arriving in it; (7) each cardiac contraction is maximal; (8) each systole is accompanied and followed by a refractory phase, during which the muscle does not respond to natural or artificial stimulation; (9) contraction of cardiac muscles lowers the conducting capacity of the muscle cells; (10) stimulation of the efferent fibers of N. vagus leads to slowing of the rate of rhythm of the heart, weakening of the force of contractions, and lowering of the conducting power of the cardiac muscle; (11) stimulation of the accelerator (sympathetic) nerves going to the heart increases the rate of rhythm and also the force of the systole; (12) drugs, like atropine and nicotine, remove the vagal influence, probably by paralyzing the telodendria of the efferent vagal axones; (13) drugs like muscarine probably act by paralyzing the telodendria of the axones of the sympathetic neurones where they enter the muscle cell; (14) the Na ions of the circulating blood favor the automatic rhythmical activity of the heart muscle cells; (15) the Na ions need to be associated with a certain proportion of Cl ions, since in pure solutions of NaCl the heart muscle cells are poisoned (Loeb)."

". . . There are at least three independent properties of the heart muscle cell: (1) power of contractility; (2) conducting capacity; (3) power of initiating primary automatic stimuli at regular intervals. According to various physiologists, there are nerve fibers influencing each of these properties: (1) those which directly influence the extent and force of the contraction (Nuel, Coats, Franck); (2) those which directly influence the conduction capacity of the heart-muscle substance (Gaskell); (3) those which modify directly the length of the stimulus periods, the frequency of the primary automatic stimuli (Ed. Weber, A. v. Bezold). Engelmann suggests that we call the first set inotropic, the second dromotropic and the third chronotropic."

The commonest disturbed rhythm is the embryocardia or fetal heart: Here the sounds and pauses are short and of the same length and the rate is increased. It sounds like a clock and is called the tic-tac rhythm; so commonly associated is this rhythm with absorption of toxins in fever or indigestion and from tobacco that it is known as the "toxic rhythm." The point of clinical importance is that this rhythm and rate alone, without any change in intensity and without any signs of cardiac disease, is not of serious moment—with other signs it may be of grave significance.

The intermittent pulse is probably the next commonest. This is not, as was supposed, a dropped beat, but an inserted beat—what Wenckebach calls "extra systoles." The heart by its property of "maximal contraction" having responded to some unusual stimulation refuses to respond again on account of its property of passing into the "refractory phase" and thus a purposeful pause takes place. During this pause the beat seems to have been dropped. Thus extra systoles are followed by the compensatory rest periods. It is now generally denied that hemisystole, that is, the right and left ventricles acting asynchronously, occurs. The continuous extrasystoles is of graver significance than that which occurs only occasionally. These continuous extrasystoles produce the gallop cadence and may be imitated by tapping in quick succession with slight pause after the first, three of one's fingers upon the table.

Delirium cordis or true arrhythmia without other signs is a danger signal—if with tachycardia and enfeeblement of impulse it is a sign of grave moment.

Tachycardia alone with its many peculiarities of sudden onset and as sudden disappearance is considered to have its origin outside of the heart. A clinical point of great assistance is the comparison of the number of beats over the heart with those over the wrist. A weak muscle may thus be detected by noting a fewer number of beats reaching the radial.

About other arrhythmias which I have not mentioned there

is still much dispute. To treat of these would be entering into the subject too abstruse for the present clinic. I would refer you to Professor Barker's compact summary of this subject ("So-called Cardiac Neuroses," *Chicago Medical Record*, May, 1901), and Professor Wenckebach's (of Groningen) "*Arrhythmia of the Heart*," translated by Snowball. Published by William Green & Sons, Edinburgh and London.

A variation in rhythm quite distinct from the foregoing is that in which jugular pulsations greater in number than those at the wrist occur. This phenomenon first noted by Adams, in 1826, and more fully treated of by Stokes, in 1846, has been found, as you know, to be associated with epileptiform, apoplectiform attacks and bradycardia. The disease is named for these observers, Adams and Stokes, who belonged to that group of brilliant Dublin clinicians among whom were Corrigan, of Corrigan's pulse, and Graves, of Graves' disease. In 1856 Stannius threw a ligature around the auriculoventricular

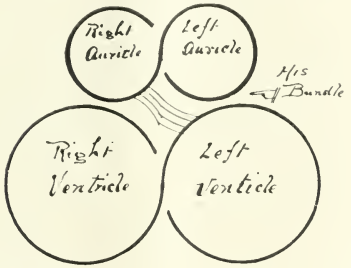

Fig. 1.—Diagram showing S-shaped arrangement of auricular and ventricular muscles and the Bundle of His, constituting the only muscular connection between auricles and ventricles

groove of a mammalian heart and noted that a less number of beats occurred in the ventricle than in the auricle. Engelmann found the same phenomenon (heart-block) occurred when the auricle was partly severed from the ventricle. In 1893 His found an anatomical connection between the auricles and ventricles, in a band of muscle. This band, which is 18 mm. long, 2.5 mm. broad, and 1.5 mm. deep, runs from the middle leaflet of the tricuspid valve close to the membranous septum and terminates at the root of the aortic valve. This constitutes the sole connection between the auricles and the ventricles. This is the bundle of His. His suspected that Stannius and Engelmann had compressed or damaged this bundle in their experiments and that Adams-Stokes syndrome or symptom complex was the disease of this muscle structure. The diagram (Fig. 1) will help us in understanding this connection between auricle and ventricles.

In 1906, Erlanger, by this specially devised clamp, kindly loaned to me by Dr. Joseph Wheelwright of the Cornell Physiological Laboratory, was able to compress this bundle and so produce at will variations of one ventricular beat to two auricular, or 1 to 3, or 1 to 4, and finally complete blocking (complete block) of the impulses when the clamp was firmly screwed down. The pace of the heart is regulated in the auricles. When the ventricles are separated from their pacemaker, they beat at their own inherent slow rate. This complete separation is called complete block. When some of the impulses can still pass from auricle to ventricle, it is spoken of as "partial block."

Demonstrations (at the Clinic):

1. The clamp.
2. The clamp in place on an uncut heart.
3. The bundle of His in the opened heart.
4. The bundle of His on the heart dissected especially to show this.
5. The ventricles from which the auricles have been separated by dissolving the fat—the only remaining connection being the bundle of His.

Fig. 2.—Sheep's heart showing the auricles removed by dissolving the auriculoventricular fat; the thin band of His fibers was the only connection which remained. This gave way on slight traction. Scalpel was not used in preparing this specimen.

The muscular arrangement of the auricles and ventricles we have learned more about recently.

By the aid of this diagram (see Fig. 1) the "S" like muscular arrangement of the heart can be best understood. These photographs (see Figs. 2, 3, and 4) of a sheep's heart (original heart shown at clinic) which was prepared without the scalpel (except that in Fig. 4, in which a single incision was made) show how completely the auricles may be separated from the ventricles and how the muscle may be *unrolled*.

The histology of the bundle of His is found to correspond to the specialized Purkinje fibers (*Die Topographie und*

Histologie der Brückenfasern, Ein Beitrag zur Lehre von der Bedeutung der Purkinje Faden, by Dr. Sunao Tawara, *Zentralblatt f. Physiologie,* May, 1905, Bd. xix, Nr. 3) and to extend very broadly, fan-shaped, into the heart wall.

DEMONSTRATION: MICROSCOPIC SECTIONS OF THESE MUSCLE FIBERS.

There are other recent contributions to our knowledge of the heart muscle, but these are the more important:

THE NERVES. In regard to angina pectoris the most important observations clinically have been made by Professor Head, and Professor Gibson, of Edinburgh. This disease has claimed for its victims such distinguished men as John Hunter, Matthew Arnold, Charles Sumner, and Dr. William Pepper, of our own school. The association between

FIG. 3.—Sheep's heart; auricles removed as in Fig. 2. The S-like arrangement can be seen rolled up. Compare this with Fig. 4, which is the same heart unrolled.

this disease and arteriosclerosis of the coronary has its parallel in that condition of arteriosclerosis of the posterior tibial known as intermittent claudication, described by Charcot. Lord Montgomery's son, when wounded in such a way as to expose his heart, was examined by Harvey, and his heart was found to be insensitive. Why should an organ insensitive to direct painful stimulation be associated with such suffering as to be termed a "pang," an "anguish," during which the individual thinks his last moment has surely come?

These diagrams after Head and Gibson will best explain this (see Fig. 5). The smaller diagram shows the spinal segment as the junction for heart and systemic nerves, stimulation of which is interpreted by the cerebral cortex, as pain, etc. Thus it is that though the seat of trouble is the heart, by "an error of psychical judgment," as Head expresses it, the pain is referred not to the heart, but to the hand and arm, which is so richly supplied with sensation. It will be seen, too, that the left side of the heart is so much more commonly connected with those spinal segments from which the left brachial plexus springs.

THE VALVES. Much has been done in experimental work regarding the valves by MacCallum, at Johns Hopkins, and Emerson at the College of Physicians and Surgeons in New York.

I will refer to only one finding which seems rich with possibilities. MacCallum found that when a mitral insufficiency was experimentally produced in a dog impulses from the left ventricle were transmitted to the pulmonary artery as indicated by a water manometer connected with that vessel and pointing *toward* the lung. Thus the capillaries of the lung offered no resistance to back pressure from the left heart to the right heart. The right heart immediately helps to relieve the strain on the left heart and the tricuspid soon yields, which further

FIG. 4.—Sheep's heart. After one cut on the surface of the ventricle the heart has been "unrolled," showing the continuous S-shaped arrangement. Compare this with Fig. 3, which is the same heart rolled up.

relieves the strain. We have here, I think, very satisfactory demonstration of what Professor Gibson has laid much stress upon—the "safety-valve action" of the tricuspid.

The clinical evidence of this is to be found in a systolic murmur in Fenwick's triangle: this triangle extends from the fourth to the sixth chondrosternal articulation on the right side with a base of two inches. A murmur systolic in time confined to this area may be taken as evidence of tricuspid regurgitation before pulsations of the liver or vessels of the neck appear, though this later is usually present. I have had this winter 6 cases, 4 of which were walking, of this compensatory safety valve tricuspid insufficiency.

In this enumeration of some additions to our knowledge of heart disease, I have touched upon a few only. Blood pressure, for example, is a subject upon which much has lately been done.

I will feel, however, our time has not been misspent if I have been able to impress two facts:

1. Rate, rhythm, and intensity taken together, not singly, may give indication of threatened compensation or incipient organic lesion of the heart or bloodvessels.

2. That tricuspid insufficiency is an effort of nature to correct left heart disease. That it occurs more frequently than we suspect and often evades us. That by detecting it early we can by instituting measures of diet, rest, etc., materially aid nature.

I wish to thank the Dean for the pleasure I have had in meeting you, and you for your attention.

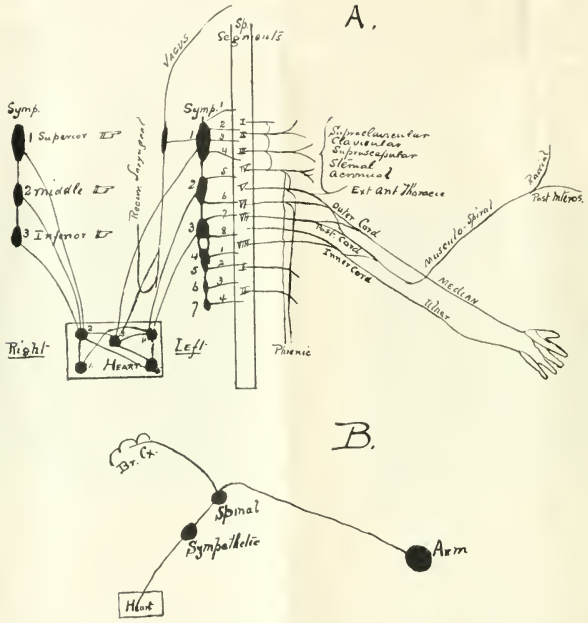

Fig. 5.—A. Diagram showing connection between cardiac, sympathetic, and spinal nervous systems. (Modified after Head and Gibson.) Heart: 1 and 5, coronary plexus; 2 and 4, deep cardiac plexus; 3, superficial cardiac plexus. Sympathetic: 1, superior; 2, middle; 3, inferior cervical ganglia; 4, 5, 6, and 7, dorsal ganglia. Spinal: I to VIII, cervical segments. Notice the greater number of connections between the left arm, chest, etc., and left cardiac ganglia than on corresponding structure on the right side. *B.* Diagram A simplified, to show that cardiac and peripheral impressions are referred to seat of all interpretations, namely, the (*Br. Ct.*) brain cortex through the common meeting point, the spinal segments.

PRESERVATION OF DEEP SENSIBILITY OF THE FACE AFTER DESTRUCTION OF THE FIFTH NERVE.[1]

By R. H. Ivy and L. W. Johnson,
Class of 1907.

Recent observations and experiments in regard to the functions of the nerves have tended to lead us far away from the conceptions which were held a decade ago concerning the forms of sensation of individual nerves. These studies have been made possible in large part by the great advances in our knowledge and in surgical technique in operations on the nerves and their ganglia. Thus, most of the cases reported as studied have been cases in which nerves were cut as a therapeutic measure, or for purposes of experiment; a smaller number have been those in which a functional loss of the nerve has been brought about by a neoplastic growth or similar factor.

The great amount of literature bearing on this broad subject, and the very numerous phases of it which have been studied, make it necessary that a paper so modest in its scope as the present one should present only a few considerations of the many which are so pertinent to the question.

This paper, therefore, is concerned chiefly with the conduction of sensory impulses from the face to the sensorium, and especially the conduction of deep pressure sensibility as contrasted with that of cutaneous sensibility to light touch, temperature, and pain sense. Up to a comparatively recent period it was considered that all sensory impulses of the face were carried by way of the fifth nerve, while the seventh nerve was concerned solely in the motor supply of the muscles to which it runs. Recently, however, the opinion has been gaining ground that we must modify this teaching to a considerable extent; and we purpose, in this paper, to present some facts in support of the changed conception of the nerve supply of the face.

Very few observers have an opportunity to study cases of uncomplicated lesions of the fifth nerve, with subsequent verification by necropsy; and, furthermore, it is exceptional that intracranial growths cause so little involvement of mentality as to permit of the delicate sensory tests required in this kind of investigation.

Head,[1] in 1905, published the results of his observations on sensory disturbances produced by section of sensory nerves of the forearm and hand. The portions of his findings which may bear on the present subject are as follows:

Complete division of the median and ulnar nerves at the wrist abolished sensations to prick, light touch, and changes in temperature, but not to pressure. "Cotton-wool rolled up into a pledget applied to the skin with some force produced a definite sensation; but if the skin was lifted the same method of stimulation entirely failed to evoke any response, a proof that whatever sensation had been previously present was due to the integrity of the underlying structures. Thus, if a part is deprived of all its cutaneous nerves it becomes entirely insensitive to prick, to touch, to all forms of temperature; but it still remains sensitive to any stimulus which jars the skin, however lightly." If, in addition to the nerves, the flexor tendons at the wrist are divided, pressure can no longer be appreciated over the area insensitive to prick, showing that pressure sensation is conveyed by fibers running in the tendons.

Head also mentions Sherrington's demonstration of afferent fibers running in the nerves which supply the muscles, and of the fact that section of motor nerves deprives the muscles and deep structures of all sensation.

From these facts Head concludes that "deep sensibility, capable of answering to pressure and to the movement of parts, and even capable of producing pain under the influence of sufficient pressure, is conveyed through afferent fibers running in the motor nerves."

The demonstration of these peculiarities of the sensory nerve supply of the trunk and limbs suggests the application of the same principles to the sensory nerve supply of the face. The idea that the seventh nerve in some way or other contains sensory fibers is not new, and tumors of the Gasserian ganglion or operations on the fifth nerve have made it possible, by eliminating the fifth, to study the relation of the seventh nerve to certain forms of sensation.

Spiller,[2] on April 24, 1906, reported before the Philadelphia Neurological Society 2 cases in which the Gasserian ganglion had been removed, the deep pressure sense in the area of of the fifth nerve remaining, while all other forms of sensation were lost. (Dana's article appeared in September of the same year.)

The importance of these investigations is clearly shown as regards the surgery of the fifth nerve. It has been noticed, not infrequently, that after operation on the Gasserian ganglion or the sensory root of the fifth nerve some sensation has been retained in the side of the face supplied by the nerve operated upon. When this has occurred, it has at times been assumed that the operation was imperfect. Two fallacies are to be considered in this connection. It is frequently forgotten that the fifth nerve supply does not extend all the

[1] Read before the Philadelphia Neurological Society, April 23, 1907.

way to the border of the lower jaw, but that a considerable area over the lower part of the cheek receives its sensation by way of the cervical nerves. The second fallacy is in regard to pressure sense; as when touch is associated with pressure, even when the latter is but slight, the tactile sensation may seem to be present when in reality it is the pressure sense that is retained. The assumption that the Gasserian ganglion has not been destroyed or the sensory root cut is more readily accepted in such cases of partial preservation of sensation on account of the well-recognized difficulty of operation on the intracranial portion of the fifth nerve. The subject is important also because after surgical intervention on the fifth nerve a certain form of sensation may be preserved so that there is not complete anesthesia even with complete destruction of the fifth nerve. In making tests we must also consider the normal variations in acuteness of perception of sensibility of the two sides of the body which occurs to a greater or lesser degree in all persons.[3]

Many writers[4]—Van Gehuchten[5] says most writers—now describe the facial nerve as in part sensory and in part motor. Retzius, and more recently von Lenhossèk,[4] have shown that the geniculate ganglion is like the cerebrospinal ganglia, and that the central processes of its cells pass into the nerve of Wrisberg. Van Gehuchten finds that at its exit from the stylomastoid foramen the seventh nerve contains undoubtedly a certain number of sensory fibers which arise in the geniculate ganglion. The nerve of Wrisberg is therefore the sensory root of the seventh nerve.

Amabolino[5] (cited by Van Gehuchten) has formed a different opinion. He believes that the peripheral processes of the cells of the geniculate ganglion pass into the chorda tympani and that none of them pass into the peripheral branches of the seventh. Van Gehuchten points out that Amabolino found about one-fifth of the cells of the geniculate ganglion normal after section of the chorda tympani, and very pertinently asks where these cells send their processes if not to the peripheral branches of the facial. Biehl[6] argues that the retention of sensation after operations on the fifth nerve is not due to regeneration of this nerve, or to an ingrowing of fibers from the fifth nerve on the opposite side of the face, or from cervical nerves, as it appears too soon after the operation, also, the limits of the area in which sensation is preserved after removal of the Gasserian ganglion correspond quite well with the limits of the area of disturbed sensation in the case of facial paralysis. Dana,[7] after testing a series of cases with lesions of the fifth nerve, comes to the conclusion that, "however true the views may be as to differentiation of afferent nerves into two kinds as applied to the body and limbs, it does not seem to apply to the head. It would seem that it is confined to the specific arrangement of spinal nerves, while the central nervous system and cranial nerves conduct sensations in a different way." To support this view he details a case in which the third division of the fifth nerve was cut as it issued from the dura, without involving any other branch. The result of this was an area of anesthesia involving the upper lip and a portion of the inside of the nose and cheek, radiating upward toward the ear halfway and within about an inch of the eyelid; also anesthesia of the mucous membrane of the mouth and tongue, of the whole inner surface of the mouth on the left side, including the gums of the upper and lower jaws and the palate to the edge of the soft palate. The area was tested by cotton, by light stroke of the camel's hair brush, by pricking with a pin, by pinching, by application of ice and very hot water in tubes, also for sense of position and deep muscular sense. An absolute loss of all these forms of sensibility was found, no matter how hard the pressure. There was no anesthesia of the ear or meatus; there was some ataxia of the muscles of the face on the affected side; he could draw the mouth to the left, but had poor control. There was also anesthesia of the periosteum of the gums. He could not tell when the mouth was open.

In view of the distinct statement that the third division of the fifth nerve was cut cleanly, without severing any other branch, it is difficult to harmonize the area of anesthesia which followed the operation with our conception of the cutaneous area supplied by the third division of the fifth nerve. The area of anesthesia, as described and pictured, encroaches deeply on the area generally ascribed to the infra-orbital and the branches supplying the nose from the second division of the fifth nerve, while the region ascribed to the auriculotemporal branch of the third division of the fifth showed no loss of sensation of any kind. The fact that there was no anesthesia of the ear or meatus seems to uphold the statement of Hunt[8] that after removal of the Gasserian ganglion and cervical nerves there still remains an area in the auricle and the external auditory canal in which sensation is preserved because its sensory nerve supply is from the seventh through the geniculate ganglion. The statement that the patient could not tell when the mouth was open is also difficult to explain. Inasmuch as the lower jaw on the left is continuous with the lower jaw on the right, forming in fact one bone, he could not open his mouth on one side without opening it on the other side also. Granting that there is loss of sense of position of the muscles attached to the bone on the affected side, will not the muscles of the sound side be moved also and give a knowledge of the position of the lower jaw-bone, whether the mouth be open or shut?

The cervical nerve supply on the affected side would also aid in giving the sense of position of the jaw.

Dana also describes a case in which a very careful examination was made of the sensory condition after complete paralysis of the seventh nerve; it apparently showed that with

paralysis of the seventh nerve there was no loss of deep sensation or sense of position.

The difficulty of studying the deep sensibility of an area where the cutaneous sensibility is not disturbed must lessen somewhat the value of this case as an argument that cutting the seventh nerve produces no loss of deep sensation. Head[4] states that deep sensation is best studied in a part where the skin is totally analgesic by reason of section of the sensory nerves supplying the part. Dana has not fulfilled this postulate, but has assumed that there was no loss of pressure sense because the patient noticed no impairment on testing through the skin supplied with sensation through the fifth nerve. The patient must be a trained and careful observer who can detect the presence or absense of the seventh nerve impulses while the fifth nerve is still intact.

The case which has given us the impetus to study sensation of the face, briefly reported, is as follows:

A. K., male, aged twenty-five years; University of Pennsylvania Hospital, March, 1907, in the service of Dr. Spiller.

The patient had considerable stupor, but was able to respond intelligently to all questions. He was able to stand and walk, but had some ataxia of gait and station. Both eyes showed a high grade of choked disk. The left pupil was considerably larger than the right; neither pupil responded to light. Left eye: This showed slight divergence. The function of the external rectus was normal; movements of the internal, superior, and inferior recti were markedly limited. No wheel movement was obtained. Right eye: In this there was loss of movement of the external rectus, and marked limitation of movement of the superior and inferior recti, function of the internal rectus being almost lost. There was complete motor and sensory paralysis of the right fifth nerve supply, which will be described in full a little later. The cause of this paralysis was a tumor growing from the dura of the right middle cranial fossa, having its centre in the location of the right Gasserian ganglion, infiltrating the dura of a large part of the middle cranial fossa, completely destroying the Gasserian ganglion and involving the motor and sensory roots of the fifth nerve to their exit from the pons; infiltrating also the dura over the central part of the petrous portion of the temporal bone, in the right posterior cranial fossa, and extending over the basilar process of the occipital bone far enough to catch the left third nerve as it passed forward into the left middle fossa. There was no question as regards the total destruction of the right fifth cranial nerve in this case.

Sensory disturbance in the area of the fifth nerve supply was as follows: Tactile sense was completely lost over the entire distribution of the fifth nerve on the right side, *provided no pressure was made;* there was loss of pain sense over the same area. Sensation was preserved along the border of the lower jaw in the area supplied by the cervical nerves. There was anesthesia of the cornea and conjunctiva on the right, with normal sensation of the left cornea and conjunctiva. A piece of paper put up the nose on the right side was not felt unless pressure was produced thereby, and did not cause lacrymation. The jaw went distinctly to the right when opened. Over the entire right side of the face, in the area completely insensitive to light touch, slight pressure was always recognized by the patient with his eyes closed, showing that the sense of pressure, even to slight stimulus, must have been produced through some other nerve supply. Owing to the condition of the patient, we were unfortunately unable to test pressure sensibility over the temporal region. The absence of pressure sensibility in this area would have been proof that this form of sensation is carried in the motor nerve to the underlying muscle, in this case the motor branch of the fifth. We also made no test of sensation in the cutaneous zone of the seventh nerve in the auricle and external auditory meatus, described by Hunt.[8]

In another case under Dr. Spiller's care a year ago the sensory root of the fifth nerve was cut because of the great pain from a tumor involving the Gasserian ganglion. The destruction of the fibers was made certain by the necropsy; and following this by microscopic study, intense degeneration of the sensory portion of the fifth was shown. The sense of touch was entirely lost over the area of distribution of the fifth nerve, while the sense of pressure was retained over the whole area. If there had been any doubt of the complete involvement of the fifth nerve by the tumor, the lesion was made complete by the operation on the ganglion, which was followed by entire loss of cutaneous sensation over the area of all three branches of the fifth nerve.

So that in all Spiller has observed 3 cases in which pressure sensibility was retained after destruction of the Gasserian ganglion.

[Note.—The importance of the lacrymal reflex in diagnosticating between organic and hysterical anesthesia of the trigeminal nerve has been pointed out by Spiller.[9] Irritation of the nostril with a probe is the most satisfactory way of testing the reflex. While the lacrymal reflex in testing by this method may be lost, yet it is possible that it may be evoked by exposure of the eye to strong light.]

Cryer has reported 3 cases of peripheral operations upon the inferior dental nerve for trifacial neuralgia, in which pain on the inner surface of the lower jaw and floor of the mouth was not relieved by section below the point at which the mylohyoid branch was given off. A second operation above the point of junction of this branch with the inferior dental nerve was followed by complete relief. This result is evidence that the mylohyoid branch, which supplies motor fibers to the mylohyoid and digastric muscles, also conveys

sensory impulses from these muscles, which from some irritation had given rise to pain

Besides the conduction of deep sensation from the muscles to which it affords motor fibers, the facial nerve is also assigned a cutaneous zone which is described by Hunt[8] as being situated within the auricle and external auditory canal. Extirpation of the Gasserian and cervical ganglia destroys the sensibility of the region about the ear, but there still remains this area in the interior of the auricle and the external auditory canal in which sensation is preserved.

Clinical, histological, and embryological investigations have shown conclusively that the facial is a mixed nerve (Hunt, *loc. cit.*). Its afferent or sensory portion is the nerve of Wrisberg. Its ganglion is the geniculate, analogous to the spinal ganglia of the posterior roots in structure; its cell type corresponds exactly to that of the spinal and Gasserian ganglia.

From the foregoing cases and facts the evidence is strongly in favor of the sensory distribution of the face being conveyed in the same way as in other parts of the body.

Our conclusions may be summed up as follows:

The fifth nerve conveys fibers of sensibility to light touch, changes in temperature, and pain from those parts generally recognized as being within the area of distribution of the said nerve.

The seventh nerve conveys fibers of deep or pressure sensibility from the muscles which it supplies with motor fibers.

The muscles of mastication, which derive their motor supply from the fifth nerve, probably are also furnished with fibers of deep sensation by that nerve.

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ANEURYSM OF THE ABDOMINAL AORTA, WITH REPORT OF A CASE AND THE POSTMORTEM NOTES OF TEN OTHER CASES.

By William Pepper, M.D.,
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Cases of aneurysm of the abdominal aorta are of sufficient rarity to warrant, I believe, my placing on record the notes of a case which presented a few interesting features, among which were the extreme size attained by the aneurysmal mass, the character and severity of the pain and the extreme emaciation of the patient. An analysis of ten other cases from the Philadelphia Hospital autopsy records has also been added to this report so that deductions can be drawn in reference to the exact location, the size, and the variety of aneurysm usually seen in this part of the aorta. The clinical histories of these cases have been destroyed.

Nunneley[1] quotes two tables that are worthy of reproduction as evidence of the approximate incidence of aneurysms of the abdominal aorta, and of their approximate relative frequency as compared with aneurysms of the thoracic aorta:

Hospital	Postmortem examinations	Aneurysms of abdominal aorta.	Approximate incidence per 1000
St. George's	17,872	32	2
Guy's	18,678	54	3
Total	36,550	86	2

[1] Inaug. Diss., Oxford, 1906. See also J. H. Bryant, Clinical Journal November 18 and 25, 1903.

Hospital.	Aneurysms of abdominal aorta.	Aneurysms of thoracic aorta.	Approximate relative frequency.
St. Bartholomew's	23	150	1 to 7
Guy's	54	271	1 to 5
St. George's	32	134	1 to 4
Total	109	555	1 to 5

Schrötter[1] in Vienna found but 3 aneurysms of the abdominal aorta in 19,300 autopsies while Osler, at Johns Hopkins Hospital, found 11 in 2200 postmortems.

The 10 cases of which I have only the autopsy notes were found on looking over about 7000 records in the Philadelphia Hospital. These apparent variations in incidence can, I believe, be explained partially by the fact that in Vienna, for example, nearly all patients dying in the hospitals are autopsied, while in America only the more clinically interesting cases reach the postmortem table. So that in order to compare such statistics intelligently one should know also the proportion of autopsies to deaths in the hospitals under consideration.

The age at which aneurysm of the abdominal aorta most commonly occurs has been estimated by most writers as being

[1] Nothnagel's spec. Path. u. Ther.

somewhat under forty years. The average of 9 cases of which I have been able to ascertain the age from the autopsy records, and including the case herewith reported, was forty-nine and one-half years. But the Philadelphia Hospital is essentially a hospital for the aged and the average age of those dying in its wards is higher than in many other institutions.

Men are much more liable to aneurysm than women and it has been shown that aneurysms of the part under discussion are no exception to this rule. In my series of cases there were 10 men and 1 woman, an incidence of but 9 per cent. among women.

Laborious occupations necessitating hard manual labor have an influence on the production of aneurysms in any part of the aorta; sudden efforts or excessive strains seem to especially have been the basis of some aneurysms of the abdominal portion. This is well exemplified in the case reported later, in which it is noted that the patient had been carrying railroad ties and had strained himself.

The etiology of aneurysm includes first and foremost atheroma from whatsoever cause produced. Probably this atheroma frequently originates from syphilis; at any rate many cases of aneurysm have had syphilis, and atheroma has been present in the vessel walls. Reference to the report following will show that the patient had had syphilis and that there was marked atheroma. The other causes of atheroma, as alcohol, gout, and various chronic intoxications probably also are at the root of some cases.

Lee Dickinson has reported 2 cases of aneurysm of the abdominal aorta caused by hypoplasia of the aorta, but this must be but a rare cause of this affection.

Abnormalities of the vessel may occasionally be at the foundation of a few cases.

Rarely direct injury may cause aneurysm in the abdominal portion, but few cases are on record.

Nunneley mentions the possibility in 1 case, the patient's occupation being that of a bootmaker, of pressure having had something to do with the formation of aneurysm. This was the occupation of the patient whose case is reported in this paper.

The site of election of aneurysm of the abdominal aorta is the Tripus Halleri of the Germans, or the triangular part of the aorta formed by the diaphragm above and the celiac axis below.

The following table taken from the St. George's Hospital series is of interest:

Situation.	Saccular.	Fusiform.	Total.
Above celiac axis	7	2	9
At level of celiac axis	4	1	5
Below celiac axis	2	—	2
Opposite first lumbar vertebra	1	—	1
Just above renal arteries	1	—	1
At level of renal arteries	2	—	2
Just below renal arteries	1	—	1
Last three inches of aorta	7	3	10

I have made a similar table from the 11 cases later mentioned which shows the situation of these aneurysms:

Situation.	Saccular.	Fusiform.	Total.
Immediately below diaphragm	2	2	3
Opposite first lumbar	1	0	1
One inch below renal	2	0	2
Opposite eighth to twelfth dorsal	2	0	2
At level of celiac axis	1	0	1
At level of superior mesenteric	1	0	1

The saccular aneurysm is the most frequent variety observed in this location. Of the 11 here reported 9 were saccular and 2 were fusiform.

The direction of extension is more commonly laterally and usually to the left side and somewhat backward according to most statistics. Backward extension is rare.

Of the 11 cases herewith reported 5 extended to the left, 1 to the right, 3 forward, and 2 being fusiform, could not be said to extend in any special direction; 7 had terminated in rupture, 4 had not ruptured.

According to Nunneley, death due to this cause occurred in 21 out of 32 cases, at St. George's Hospital; in 43 out of 54, at Guy's Hospital, and in 20 out of 24, at St. Bartholomew's Hospital. Among Crisp's 54 cases which he tabulated, death was due to rupture in 34. The 7 cases from the Philadelphia Hospital series here quoted showed that

Rupture into the retroperitoneal tissues took place in	3
Rupture into the peritoneal cavity took place in	1
Rupture into the left lung took place in	1
Rupture into the lesser peritoneal cavity took place in	1
Rupture into the right pleural cavity took place in	1
Total	7

Among 32 cases of the St. George's series

Rupture into the retroperitoneal tissues took place in	11
Rupture into the peritoneal cavity took place in	5
Rupture into the left pleural sac took place in	3
Rupture into the left lung took place in	1
Rupture into the first part of the duodenum took place in	1
Total	21

In Osler's[1] 16 cases rupture followed wiring and electrolysis in 4 cases.

Rupture of aneurysms of the abdominal aorta is thus shown to be a very frequent termination, which can be readily understood, when one considers the case with which that portion of the aorta can expand and that it is not surrounded by firm structures.

Symptoms. Unfortunately the 10 cases here abstracted from the autopsy records of the Philadelphia Hospital, do not allow us to draw any deductions as to the symptoms in these cases, the clinical notes having been destroyed. The 1

[1] Lancet, October 14, 1905.

case reported later in full with notes on the postmortem findings ran a perfectly typical course and will be discussed subsequently.

In the great majority of cases of aneurysm of the abdominal aorta pain is preëminently the most constant and striking symptom. It is very severe and violent in character at times, or more frequently dull and boring, with occasional exacerbations of acute suffering. In Osler's 16 cases it was present in 13 and was persistent and often was of an agonizing character. It was present in 27 of the 32 cases in the St. George Hospital series. The pain in the case reported in this paper was intense and required large doses of opiates. Flexion of the left leg at times gave temporary relief.

Erosion of the vertebræ, a not infrequent occurrence, gives rise usually but not invariably to a dull, aching, boring pain, very persistent and augmented by intense paroxysms. The spinal nerve roots are stretched, broken or compressed, during the process of erosion.

The intervertebral disks resist in nearly all cases this erosion which is seen in the bones. In those cases in which rupture of the sac takes place there is usually a tearing, lancinating paroxysm which later, depending upon the structures involved, may simulate the pain of renal or biliary colic, appendicitis, pleurisy, and other conditions. Gastric or intestinal symptoms are sometimes present, depending on the size and consequent pressure and displacement of the viscera.

Maylard[1] reports a case in which he discussed the advisability of operation with the hope of relieving a patient suffering from painful attacks of mucous colitis, but a tumor appeared posteriorly, followed by sudden death, and the case proved to be one of abdominal aneurysm.

Emaciation has been mentioned by some observers as being fairly constant. Other occasional symptoms are hematemesis, hemoptisis, jaundice, intermittent claudication, anesthesia and paraplegia, edema, hemorrhage from the bowels, and the retention of urine.

The diagnosis of aneurysms of the abdominal aorta is often most uncertain. A glance at the clinical diagnoses, where given, in the cases upon which this paper is based will show this plainly.

Clinical Diagnosis.

Aneurysm of abdominal aorta	5
Cirrhosis of liver and heart disease	1
Cirrhosis of liver and interstitial nephritis	1
Uremia	1
Arteriocapillary fibrosis	1
Not stated	2
Total	11

Other writers have quoted similar results.

Bryant mentioning among erroneous diagnoses the following: Malignant tumors lying in front of the aorta, renal calculus, lead colic, spinal caries, sarcoma of the kidney, nephritis, perinephritis, pneumothorax, pleuritic effusion, epithelioma of œsophagus, malingering, chronic intestinal obstruction, etc.

Diagnosis. The diagnosis depends upon the presence of a definite tumor that can be grasped and which has an expansile pulsation. Other physical signs there are, but none of much value.

Pulsation. Inspection may show pulsation in the epigastrium, this may be due, however, to an abnormally pulsating aorta, which has undoubtedly often led to mistakes in diagnosis. Osler says, "I suppose there is no young physician who has not diagnosticated as aneurysm of the aorta the preternatural pulsation of the vessel, as Allan Burns[1] calls it." This pulsation has a number of causes, and is more common in women, while aneurysm is much more common in men. It is, therefore, wise not to make a diagnosis on this sign alone, especially in women. In these cases Osler states that it is well to bear in mind (1) That the pulsation occurs in nervous or hysterical women or in neurotic or hypochondriacal males. In mild forms it is common. (2) The subjective sensations may be pronounced pain, abdominal distress, nausea, sickness, constipation, and in some instances the vomiting of small quantities of blood and the passage of blood in the stools. (3) The degree of visible and palpable pulsation may be extreme. The abdominal aorta is easily palpable and may be grasped in the fingers. It is sometimes tender; no definite tumor is felt. With such anemia a thrill may be present. A soft systolic bruit may be heard, even without any pressure of the stethoscope. A mistake is not likely to occur if it is remembered that no pulsation, however forcible; no thrill, however intense; no bruit, however loud —singly or together— justify the diagnosis of an aneurysm of the abdominal aorta, *only the presence of a palpable, expansile tumor.*

Various abdominal growths, such as carcinoma of the stomach, cysts, and solid tumors of the pancreas mesentery or retroperitoneal lymph glands may give a most confusing transmitted pulsation. Allan Burns remarked that "a tumor placed over the course of an artery, and attached to it, always pulsates more strongly than the vessel." It is a difficult matter in other portions of the body also to differentiate true from transmitted pulsation; I recently saw a case in point.

A man with either a ganglion of the wrist over the radial artery or a small aneurysm of that vessel. In such a situation one would think the diagnosis would be easy and yet a number of competent men gave varying opinions, and it was never positively determined. I have heard several other similar differences of opinion expressed about cases with possible aneurysms located in parts of the body much more accessible to examination than the abdomen.

[1] Brit. Med. Jour., July 28, 1900.

[1] Observations on Diseases of the Heart, etc., 1809.

Severe anemia is often accompanied by pulsation or throbbing of the arteries, especially of the abdominal aorta. Examination of the blood and inspection of the superficial arteries should lead to a proper diagnosis.

Aortic regurgitation gives rise to a forcible throbbing of the aorta, as well as of other arteries of the body, and can in some cases give rise to uncertainty.

Cardiac enlargement, if excessive, may cause marked epigastric pulsation.

Tumor. This sign in itself is not of much value and probably often leads to mistaken diagnosis; the majority of cases have a palpable mass in the abdomen, but on account of the extension of these aneurysms, in a lateral and backward direction, at times the tumor cannot be felt.

Bruit. Sometimes present and sometimes absent and at times caused by other conditions than aneurysm.

Emaciation. In a number of cases this has been more marked than would be expected, and has, therefore, been included by some writers as a symptom. In the case I am reporting the emaciation was very marked and rapid in its appearance.

Retardation of the *femoral* pulse has also occasionally been noted.

The diagnosis of aneurysms of the abdominal aorta from those of other arteries in the abdomen is usually a very difficult one, especially so when the aneurysm is situated in a branch close to its origin from the aorta. The only difference being that aneurysms of the smaller arteries usually are not so large, are more often more laterally placed, more movable, more easily grasped and more superficial, but at times cannot be differentiated from those of the aorta. One of the cases from the Philadelphia Hospital series was possibly of the celiac axis, but it also involved part of the anterior wall of the aorta and has, therefore, been included.

Treatment. Occasionally a case of healed aneurysm of the abdominal aorta is found at autopsy, but this is very rare, the great majority of cases either with or without treatment progress steadily to a fatal termination, usually living between one and two years after coming under observation.

Tufnell's treatment prolongs life certainly, but cures very rarely; the same can be said of subcutaneous injection of gelatin.

Ligation has been tried about fourteen times. W. W. Keen[1] reported a case that lived for forty-eight days, the longest on record. He also gives a full list of the literature upon this subject.

Compression of the aorta, devised in 1864, by Murray,[2] has been tried about ten times with five successful cures. Keen has suggested an improvement, to prevent the injury done the intestines by pressure, which consists in applying the compression by means of a clamp on the aorta itself, the abdomen having been opened previously.

Needling and Galvano-puncture are only applicable to cases where the sac is in contact with the abdominal wall and then usually the aneurysm is too large to hope for a cure.

Moore,[1] in 1864, recommended the introduction of fine wire into aneurysms of the aorta with the hope of forming a clot in the sac. About 9 cases of aneurysm of the abdominal aorta have been treated in this manner, with 2 cures.

D'Arcy Power,[2] in 1903, reported a case in which he made use of an apparatus devised by G. H. Colt, consisting of a sort of cartridge composed of closely packed wire which was pushed through a cannula, previously introduced into the sac of the aneurysm, and there allowed to expand, thereby ensuring a better disposition of the wire network and reducing very greatly the time formerly used in inserting many inches of wire through a very fine cannula.

Burresi,[3] in 1879, made use of a suggestion of Corriadi's and passed a constant current through the wire introduced into the aneurysm with the idea of forming a clot more rapidly around the wire network. In at least 13 cases, 2 of which were cured, has this been tried.

The case reported in this paper was in no way a suitable case for such radical treatment, as reference to the history will show.

Report of Cases.

John L., male, white, born in Ireland, aged forty years, shoemaker. Admitted to the surgical wards of the Philadelphia Hospital, service of Dr. Chas. H. Frazier, on August 11, 1903. The chief complaint was difficult urination. Bedsore on left buttock. Pain in left lumbar region. Physical examination negative except for slightly enlarged liver and the presence of a tumor mass in left side of abdomen extending from costal margin downward to iliac crest. An expansile pulsation of this mass was felt, but on auscultation no bruit could be heard. The patient was transferred to Dr. Stengel's wards, and it is to him that I am indebted for the opportunity of reporting this case. The following history and notes were written August 19, 1903, in the medical ward:

Family History. Not of importance. No malignant disease nor tuberculosis.

Past Medical History. Had syphilis when a young man; treatment only lasted about two months. No other severe illness. About a year ago, began failing in health, lost weight rapidly, and suffered from pain in lumbar region, which is stated to have come on after he had strained himself carrying railroad ties. This pain ran down left hip, thigh, and leg.

[1] Phila. Med. Jour., 1900, p. 470.
[2] Edinb. Med. Journ., 1868, xiv, pp. 33 to 47.

[1] Med.-Chir. Trans., 1864.
[2] Ibid., 1903, vol. lxxxvi, p. 363.
[3] Lo Sperimentale, April, 1879.

and was relieved by flexing the limb. Pain was at first dull, but became sharp and shooting in character, and two months ago became so severe as to prevent his walking. As shoemaker he was compelled to press his last against the pit of his stomach but never suffered from this, except that shortly before he stopped work his abdomen felt rather full. The difficulty in urination had existed for some weeks before his entering the hospital.

Physical Examination. Very thin, wasted man, no glandular enlargements. Thorax negative except for a slight systolic murmur at apex. A distinct fulness in left flank could be seen. A mass the size of a fist could be felt close under the skin which was stretched quite tense. Over this mass the percussion note was dull. The dulness did not run above the costal margin, and extended only about an inch to the right of the median line; below it dipped behind the crest of the ileum while it extended to the left around to the spine. No bruit could be heard over this mass. The femoral pulses were equal and not delayed.

August 20. Examination of the blood showed red cells, 2,620,000; white cells, 4100. Urine contained albumin.

24*th*. Left thigh cannot be extended without pain, muscles wasted. Patellar reflex absent. Babinski's reflex absent.

September 2. Patient fairly comfortable. Pain not so acute in character.

5*th*. Pain has increased markedly in the thigh and abdomen, requiring opiates. The tumor is increasing posteriorly rapidly in size. A bruit can now be heard.

5*th*. Paroxysms of pain. Large doses of opiates. Tumor is still larger, bulging considerably posteriorly to the left of the spine.

7*th*. Pain slightly less. Morphine reduced. Hemoglobin, 50 per cent.; red cells, 2,800,000; white cells, 5200.

9*th*. Still has pain. The bulging posteriorly is growing still larger, the skin being edematous and discolored. Pulsation is very plainly visible.

10*th*. The mass is now much larger posteriorly than anteriorly. Skin becoming darker.

11*th*. Tumor mass still larger posteriorly. Measures nine by five and one-half inches. No tenderness elicited by pressure over spine. Patient growing more emaciated. Urine: acid, 1017, albumin +, no sugar, few hyaline casts, leukocytes, epithelium + · , urates.

Patient died on September 18, at 6.35 P.M., from progressive weakness; the mass posteriorly not having ruptured externally.

Clinical Diagnosis. Aneurysm of abdominal aorta with retroperitoneal rupture and formation of large adventitious sac.

The autopsy was performed at 9.20 A.M., on September 19, by Dr. A. Ellis, Assistant Pathologist to the Philadelphia Hospital.

The body of a markedly emaciated adult male. The left side of the abdomen is prominent from slightly below costal margin to pubis, the maximum point of prominence, projected about 5 cm. and was to the left and slightly above the umbilicus. This prominence continues toward the left between the ilium and the costal margin and becomes more pronounced posteriorly, where there is a globular swelling occupying the entire left lumbar region. The maximum elevation here being approximately 8 cm. On the outer part of the left thigh over the greater trochanter there is an excavated ulcer about 4 by 6 cm. in diameter, and about 8 cm. below this is an irregular area in which the superficial portion of the skin

Photograph taken a few days before the patient's death; showing the large projecting mass to the left of the spinal column.

has sloughed, and extending from this, over the neighboring anterior part of the thigh is a discolored area 9 cm. in length. The left foot is markedly edematous and the left leg is also edematous, but to a lesser degree. The edema also extends slightly above the knee. The right leg is not edematous. There is a slight edema of both hands, more marked in the right. The coils of intestine are firmly bound together with old adhesions. The liver is firm and adherent to the abdominal wall. The left kidney is displaced forward by a large globular mass situated posteriorly. Both pleurae contain old adhesions, more marked on the right side. The pericardium contains 60 c.c. of clear fluid. The heart contains a small

amount of fluid blood. The walls of the left ventricle are slightly thickened; the muscle is pale in color. The endocardium is somewhat grayish in color. The mitral and aortic valves are slightly thickened. The aorta is markedly atheromatous, and light in color. The pleurae are not thickened. The cut surfaces of the lungs are light in color and abnormally dry. The spleen is small and shows some thickening of its capsule. The intestines and stomach appear normal excepting for the adhesions noted. The liver has a thickened capsule. A cut surface shows alternating gray and red markings. The kidneys show a slightly swollen cortex, light in color. At points the cortex is slightly thin. Abdominal aorta: Immediately below the diaphragm there is a distinct bulging of the aorta for a distance of 10 cm. This bulging is continuous on either side into a sac which extends on the right side outward and downward a distance of 10 cm. and on the left side is continuous with the large mass previously mentioned. All the branches of the aorta, except the small posterior ones immediately involved, are normal. On dissection, the mass in left side of abdomen is found to be composed of blood, the major portion of which is in the shape of laminated clots some of which show beginning organization. The opening in the aorta is directly posterior, has rounded margins, and is 3.5 cm. in length. The bodies of the eleventh and twelfth dorsal and first lumbar vertebrae are markedly eroded; the blood stream at this point having been directly in contact with the bone.

This case presented, therefore, in short, the following points of interest: There was a history of syphilis as well as that of pain coming on after excessive straining. The pain became more and more pronounced. A mass was found in the left hypochondriac region which later protruded on the same side posteriorly, was expansile, and had a bruit that could be heard over it. There was marked emaciation. Death from exhaustion.

PHILADELPHIA HOSPITAL POSTMORTEM CASES.

The autopsy notes of the 10 cases found in the postmortem records of the Philadelphia Hospital here follow:

Edward W., male, aged forty-seven years, colored, New Jersey. Admitted May 1, 1895; died, May 1, 1905.

Clinical Diagnosis. Interstitial nephritis; cirrhosis of liver.

Pathological Diagnosis. Interstitial nephritis with acute exacerbation. Chronic, passive congestion of right kidney. Old pleurisy. Hypertrophy of left ventricle. Aneurysm of abdominal aorta, involving cardiac axis, the renal, superior, and inferior mesenteric arteries. Dr. J. D. Steele, Pathologist.

Somewhat emaciated. Abdomen markedly retracted.

Immediately below pancreas, opposite origin of seventh costal cartilage, is a round tumor lying behind the peritoneum and carrying upon its surface the inferior vena cava and the nerves of the solar plexus. Tumor measures 6 cm. in antero-posterior diameter, and 8 cm. in vertical diameter. It is round, about size of orange. Tumor about opposite twelfth dorsal vertebra. Heart muscle of good texture. Considerable atheroma of aorta above aortic valves, which are not affected. Slight thickening of edges of mitral valve, competent.

Aneurysm of abdominal aorta opposite the first lumbar vertebra. Lying on tumor on its upper edge is the pancreas. No change in peritoneum covering the tumor. The renal vein of the left side crosses the tumor to join the inferior cava and is dilated so as to measure 2 cm. at its widest portion. From the aorta, immediately above the tumor, the celiac axis is given off and is adherent to the tumor as far as its apex, with all of its branches. The left renal artery comes from the aorta (trunk), just below the opening. The opening of the artery into the aorta is clean and rounded and measures 3 by 2 cm. The long diameter runs in the same direction as the artery. The artery is filled with red and firm coagula with considerable fibrin running through the mass as a reticulum. The adventitia of the aorta is stripped off down to the artery and there it is seen to form the wall of the aneurysm on the extreme apex. While the rest of the wall seems to be formed by all the coats of the artery.

Mary R., female, aged seventy-four years, white. Admitted September 2, 1889; died July 4, 1891. Dr. Vansant attending physician. Autopsy by Dr. Cattell. Cause of death, uremia.

On opening abdomen there was seen to be an elevation occupying a position to the left of the median line. The tumor is four and three-quarter inches in length. Eight inches in circumference at the greatest part and six inches at the lower portion. Kidney-shaped, and springing from left median arteries surface of abdominal aorta an inch below renal arteries and extending down to common iliacs. Posterior wall of aorta is in good condition with the exception of much atheroma and atheromatous plates. On opening aneurysmal tumor the wall at its greatest thickness a little less than one-sixteenth of an inch. There then came a layer of dark-colored fibrin which grew lighter as it approached the centre. This organized lamina extends toward the centre one and seven-sixteenths of an inch at thickest point and then becomes dark red in color, showing that the blood at this point had become but recently organized. Depth of recently organized matter was one and one-quarter inches at greatest diameter. Heart normal in size. Aortic valves showed some calcareous roughening at base, but still were competent. Mitral valve showed much atheromatous change in the auricular aspect. The whole aorta removed for museum. Photo-

graph taken. The lower part of aneurysm extends below the bifurcation.

Pablo C., male, aged thirty-five years, Cuban. Admitted February 15, 1895; died April 20, 1895.

Clinical Diagnosis. Cirrhosis of liver and valvular heart disease.

Pathological Diagnosis. Dilatation of heart, chronic parenchymatous nephritis; nutmeg liver; aneurysm of aorta.

Heart dilated. All cavities distended with blood. Mitral valves incompetent. Mitral valves (anteriorly) slightly thickened. Orifice dilated, weight 470 gm. Large arteries atheromatous. A large aneurysm of abdominal aorta 8 cm. in diameter extends from eighth dorsal to twelfth dorsal vertebra. Projects forward from anterior surface of aorta. The lumen of aorta is about normal; in the anterior half of aneurysm organization has taken place and a distinct laminated structure is clearly made out. The posterior portion is filled with a large red clot.

Washington D., male, aged forty-three years, colored; Philadelphia. Admitted February 27, 1895; died March 16, 1895.

Clinical Diagnosis. Aneurysm of abdominal aorta.

Moderate emaciation. On opening abdomen blood-stained serum escaped together with clotted blood. A firm clot measuring one quart. Clots distributed throughout abdomen. Beneath left lobe of liver, an aneurysmal sac, about the size of a fist, also along the lesser curvature of stomach which was pushed over by it. The rupture was along the left border of the tumor and into the lesser peritoneal cavity, blood having escaped into general peritoneal cavity through the foramen of Winslow. Aneurysm evidently sprang from the celiac axis, although the trunks of that vessel were not demonstrable. It was filled with an organized clot. The aorta below the aneurysm was apparently unaffected by it. The walls of the aorta were throughout apparently normal. About an inch and a half of the aorta was involved on its anterior surface. There was no clot in the aorta. The aneurysm lay upon the aorta, with no bulging of aorta at sides.

Heart is small, glassy; superficial vessels tortuous. A milky patch on left ventricle. Valves normal. Thoracic aorta normal.

Hugh R., male, aged forty-five years, white; Pennsylvania. Admitted August 24, 1895; died November 5, 1895.

Clinical Diagnosis. Abdominal aneurysm.

Well nourished. Abdominal cavity contains small, black clots of fluid blood. Stomach lies almost exactly vertically. Liver also. Left lobe pushed up, the right down. Left pleural cavity contains about one-half pint of clear fluid. Right cavity also contains clear fluid. Pericardial sac contains about ℥vi clear fluid. Spleen compressed by aneurysm forms part of anterior and upper capsule of aneurysm. Spleen 15.5 cm. by 9 cm.

Left kidney in part embedded in clot. Is flattened, resembling a spleen. Pancreas forms part of wall of aneurysm. Liver firm. Left extremity of left lobe atrophied by pressure.

Thoracic aorta somewhat dilated, a few patches of atheroma. Abdominal aorta quite atheromatous, especially in region of rupture into aneurysmal sac. Bodies of twelfth dorsal and first lumbar vertebræ extensively eroded, second lumbar less so. The lower ribs also somewhat eroded. Intravertebral disk between twelfth dorsal and first lumbar eroded down to dura mater. The whole left half of abdominal cavity down to within two inches of crest of ilium filled with a moderately firm mass carrying in front of it the colon, which is dissected off of it only with difficulty. Anterior wall of mass composed of peritoneum. Kidney, pancreas, spleen, and diaphragm. Mass measures in length 30 cm., in breadth 18 cm., and in thickness 10 cm.; it is so adherent laterally and posteriorly that it can be gotten out only by dissection of tissues. Composed centrally of firm laminated blood clot, peripherally of soft, black clot, merging into the laminated clot; especially is the black clot prominent in the lower part of the mass. The rupture in the abdominal cavity has apparently taken place posteriorly and a little also at the lower border of the spleen. This cavity (aneurysmal) communicates with the aorta by an opening in the posterior wall 7 cm. in length, directly opposite the superior mesenteric artery. This opening has *firm,* rounded, and smooth edges directly continuous with the lining of the aneurysmal sac.

Mathew D., Ireland; Dr. J. B. Walker. Died March 25, 1885.

Pericardial sac bulging. Heart aorta slightly dilated, presented itself prominently even on uncovering the heart. At root of pulmonary artery, a small saccular dilatation above origin of aorta anteriorly.

Aneurysm of abdominal aorta from diaphragm to iliac artery filled with old coagula and its lumen occupied with recent clots. Shape of aneurysm fusiform. No erosion of vertebræ. Aorta much thinned at its commencement. Atheromatous changes in aorta capable of admitting small chestnut. Aorta roughened. Some calcified plates on arch. Left auricle much dilated; the mitral orifice dilated, admitting more than three fingers. Slight thickening of valves. Left ventricle thickened, slightly dilated.

John B. Admitted November 11, 1867; died January 25, 1868. Pathologist, Dr. Pepper.

Heart unusually small for an adult male. Weight nine and three-quarter ounces. Tissue firm, of good color. Aortic valve containing a few specks of atheromatous matter, but

flexible. Mitral valve the same. Right ventricle walls remarkably thin and flabby. No atheroma of tricuspid valve. Pericardium enlarged. Its insertion into aorta forced upward four inches from heart, but apparently healthy. Aorta dilated just above the valves, measuring more than two inches in width. Its walls perhaps slightly thickened, but still smooth, pliable, and but very little atheroma. The vessels arising from arch also quite healthy. In descending part, walls became more rigid. The aneurysm involved the aorta just below the diaphragm. Spherical in shape, flattened anteriorly, larger upon right than left side of spine. Diaphragm was closely adherent to it on the right side and the aneurysm bulged upward into the right pleural cavity, at the inferior part of which, close to the spinal column, there was an ulcerated opening, one and one-half inches in diameter, through which the fatal hemorrhage amounting to a pint had occurred.

The aneurysm measured in its circumference twenty-one inches. It was very closely attached to and embraced the spinal column from a level of the second lumbar to level of ninth or tenth dorsal.

Upon pressing finger in through the ulcerated opening, above mentioned, it came in contact with necrosed fragments of vertebral bodies, and it was evident that extensive absorption and necrosis of the vertebræ, included in this limit, had occurred. The aneurysm seems to have arisen entirely from the posterior wall of aorta. The anterior wall can be traced remaining comparatively healthy, and the vessels of celiac axis were merely moderately atheromatous.

The abdominal aorta was of natural size, its walls somewhat atheromatous, as well also the iliac arteries. The dorsal curve was much increased. On laying open anterior wall of aorta, over seat of aneurysm, this was found merely to present patches of atheroma. There was an opening nearly three inches in diameter in posterior wall of aorta, with smooth, rounded edge, leading into cavity of aneurysm. This was at least four-fifths filled with exceedingly firm, white clots, which were so compact as to resist laceration with the finger and scarcely to be capable of separation from wall. The remaining space of the sac was a shallow fossa on the surface of this old clot, and here also clots, though more soft and recent, were contained. The upper pair of vessels, coming off from aorta below inferior mesenteric, were comparatively healthy, the right one having, however, its middle coat very much thickened. The second pair were excessively atheromatous.

On right, in upper part of psoas muscles, there was a cystic cavity with quite well-defined wall of altered muscle and condensed cellular tissue, about one inch in diameter, with dark-brown, grumous, pulpy contents. It was very easy to pass a probe from this into the sac of the aneurysm, but not without lacerating a softened and readily torn septum, so that probably there was no direct communication. On left side there was a small cavity, size of a hazel-nut, with similar contents, and one larger cavity with firm, distinct, yellowish, fibrous walls. These were all formed in the substance of the psoas muscle.

John R., male, aged sixty years, white; Irish. Admitted January 20, 1899; died April 22, 1899. Attending physician, Dr. D. E. Hughes; pathologist, Dr. Jameson.

Clinical Diagnosis. Aneurysm of aorta.

Pathological Diagnosis. Peritoneal hemorrhage; chronic, fibrinous pleurisy (left); emphysema; tuberculosis (right apex); cardiac hypertrophy (eccentric left); chronic parenchymatous nephritis; abdominal aneurysm with erosion of bodies of spinal vertebræ and ribs; moderately emaciated, poor muscular development; congulated blood filled the spaces between the folds of intestines; in the pelvis some in region of the right hepatic flexures, considerable above the stomach and along the line of the descending colon; a large hematoma occupied the region behind the descending colon down almost to the pectineal line; a moderate amount of blood was found in peritoneal cavity.

Heart hypertrophied; valves normal; slight atheromatous change in beginning of aorta; thoracic aorta shows moderate amount of atheroma; abdominal aorta has in it an opening over the tenth and eleventh thoracic vertebræ in the posterior surface, about one and a half inches in length and one inch in breadth; this opening leads into a large space bounded by the anterior and left lateral surfaces of the ninth, tenth, eleventh, and twelfth thoracic and first lumbar vertebræ, and the cavity also extends down beside the spinal column, and the outer wall is about three inches away from the spinal column; this cavity contained a large amount of fibrinous material in shreds, but none in laminæ.

The interosseus cartilages of spinal column show very little atrophy from the pressure, but the bodies of the above-named vertebræ are irregularly atrophied in places one-quarter inch and in other places down to the spinal canal. The ninth, tenth, eleventh, and twelfth ribs on left side are eroded free from spinal column. The aneurysmal cavity extended between the tenth and twelfth at least one-quarter inch beyond the posterior limits of the ribs. Through the eleventh vertebral body a probe readily passed into the spinal canal.

Robert N. S., male, aged seventy-four years, white; German. Admitted June 2, 1896; died July 27, 1896. Attending physician, Dr. Eshner; pathologist, Dr. Sailor.

Clinical Diagnosis. Arteriocapillary fibrosis.

Pathological Diagnosis. Sacculated aneurysm of descending arch of thoracic aorta; sacculated and dissecting aneurysm of abdominal aorta, with rupture in superior anterior wall; retroperitoneal hemorrhage; general arteriocapillary fibrosis; myomalacia cordis; atheromatous infiltration of endocardium;

chronic purulent bronchitis; tuberculous infiltration of apices; pulmonary emphysema and edema; soft, splenic tumor; fibroid degeneration of right adrenal body; contracted kidney of arteriosclerosis; chronic pyelitis and cystitis; fatty infiltration of liver; slight cirrhosis.

Slender but moderately well-nourished man. Paniculus adiposus. A large retroperitoneal hemorrhage occupying chiefly the left side of abdominal cavity and staining mesentery as far as kidney. This hemorrhage infiltrated all the retroperitoneal structures as far as the pelvis. Clot was soft, dark red, and on pressure exuded serum. A huge mass of blood infiltrated the perirenal fat. Abdominal aorta appeared much distended. The splenic artery was exceedingly tortuous and atheromatous, as were all the arteries of the abdominal cavity.

Heart. Vessels on surface moderately tortuous. Tricuspid admits four fingers; soft, slight thickening. The bases of mitral valve infiltrated with atheroma. Chordæ tendineæ contain calcareous nodules. Mitral admits two fingers. Edges of valves moderately thickened. Myocardium friable and soft. Aortic valves sclerotic with calcareous nodules; coronaries are rigid, calcareous tubes. Just below the point of origin of vessels of arch of aorta there was a dilatation about 5 cm. in diameter. Walls of this dilatation were dense and atheromatous and in upper part had torn during the removal.

As there was no blood in the neighborhood, this aneurysm had not ruptured.

The whole of the descending aorta and arch showed atheromatous infiltration with numerous areas where intima had been destroyed by ulceration. In the abdomen the celiac axis was considerably dilated and its branches tortuous and rigid. Below the axis the renal arteries emerged and just below these there was a large, saccular dilatation of aorta extending downward to just above the bifurcation. This sac would easily contain an enclosed fist and was lined with laminated clots, some of which could be seen on external surface. A large, ragged opening in upper anterior aspect of aneurysm communicating with retroperitoneal space. Spinal column showed slight bowing posteriorly to the left and exostosis on bodies of the vertebræ.

John H. W., male, aged twenty-eight years, colored. Admitted September 29, 1883. Attending physician, Dr. Curtin; pathologist, Dr. C. P. Henry.

Thorax. Extensive and firm old adhesions on right side. Left lung normal except at base, where its parenchyma was fused with the diaphragm and upper wall of the abdominal aneurysm below described. A number of clots were found in the air cells, here indicating a hemorrhage from the aneurysm which opened into the lung at this point.

A large part of the abdominal cavity was occupied by a large, fusiform tumor which, on examination, proved to be a large aneurysm of the abdominal aorta. The enlargement began just below the insertion of the crura diaphragmatica and was situated behind the stomach and beneath the pancreas. It was in shape an elongated ovoid, its length being about ten inches and its circumference about eight inches at largest point. It was filled with clots mostly postmortem, which were found to weigh one pound nine ounces. At its upper left margin its wall was adherent to remains of diaphragm and left pleura, and at this point a rent was found two inches in length communicating with the air cells of the left lung, in which latter structure also clots were found. On passing the finger through the opening, whose walls tore very easily, through a mass of clots, the carious and eroded bodies of the vertebræ could be readily felt. Over the most prominent point of the tumor the pancreas was adherent and prominent, being enlarged and hardened.

Cause of death: Aneurysm of abdominal aorta.

Name.	Sex.	Age.	Color.	Condition of wall of aorta.	Situation of aneurysm.	Type.	Rupture.	Remarks.
John L.	M.	40	W.	Markedly atheromatous	Immediately below diaphragm extending 10 cm.	Saccular	Yes	Enormous false sac. Great emaciation
Edward W.	M.	47	W.	Considerable atheroma	1st lumbar	Do.	No	Round, 6–8 cm.
Mary R.	F.	74	W	Much atheroma. Atheromatous plates	1 inch below renal down to iliac arteries	Do.	No	4½ inches in length. 8 inches in greatest circumference
Paldo C.	M.	35	W.	Atheromatous	8th to 12th dorsal	Do.	No	8 cm. in diameter
Washington D.	M.	13	B.	Normal	Celiac axis	Do.	Yes	Rupture into lesser peritoneal cavity. Aneurysm size of fist
Hugh R.	M.	45	W	Abdominal aorta quite atheromatous	Opening directly opposite superior mesenteric artery	Do.	Yes	Mass 30 to 18 to 10 cm.
Matthew D.	M.	?	W	Very much atheroma	Diaphragm to iliac arteries	Fusiform	No	
John B.	M.	?	W	Slight atheroma of abdominal aorta	Just below diaphragm	Saccular	Yes	24 inches in circumference. Ruptured into right pleura
John R.	M.	60	W	Moderate atheroma	10th and 11th thoracic	Do.	Yes	Rupture into peritoneum
Robert N. S.	M.	74	W	Much atheroma	Just below renal arteries	Do.	Yes	Rupture into retroperitoneal space
John H. W.	M	28	B.		Just below crura. Extended 10 inches	Fusiform	Yes	Rupture into left lung

BOOK REVIEWS.

THE PRACTITIONER'S MEDICAL DICTIONARY. An Illustrated Dictionary of Medicine and Allied Subjects, Including all the Words and Phrases Generally used in Medicine, with Their Proper Pronunciation, Derivation, and Definition. By GEORGE M. GOULD, A.M., M.D., author of *An Illustrated Dictionary of Medicine, Biology, and Allied Sciences, The Student's Medical Dictionary,* 30,000 *Medical Words Pronounced and Defined, Biographic Clinics, The Meaning and Method of Life, Borderland Studies,* etc.; Editor of *American Medicine.* Pp. 1043, with 388 illustrations. Philadelphia: P. Blakiston's Son & Co.

Gould's experience as editor of medical dictionaries is very extensive, and probably more of his medical dictionaries are in use today among English-speaking physicians than of any other lexicographer: the publishers state that more than 200,000 of his various dictionaries are scattered among the profession in many parts of the world, thus testifying to their usefulness in the great cause of medical science and progress.

This book is new in every respect and detail. Its object is to supply the practitioner with trustworthy, modern definitions of essential medical words and terms; it is based on recent medical literature. Of valuable and important novelties, which have been adopted in this volume, we wish to mention the addition of the metric system of weights and measurements to the older and more common forms, the additions and changes of the new (eighth decennial) U. S. Pharmacopœia and the new anatomical nomenclature adopted by the Basle convention.

A few errors have crept in, but for a first edition, we must say, very few. Among them deserves mentioning on page 732, near the bottom: Position, Fowler's, that obtained by elevating the foot of the bed 24 to 30 inches; this should read the *head* of the bed.

Eyestrain has not been defined at all, but that is probably due to Gould's supposing everyone to be as familiar with it as he himself.

Many valuable anatomical illustrations are scattered through the book. The general make-up of the book is pleasing and attractive, and no physician will regret adding it to his library. E. L.

PRIMER OF PSYCHOLOGY AND MENTAL DISEASE. By C. B. BURR, M.D., Medical Director of Oak Grove Hospital, Flint, Michigan, for Mental and Nervous Diseases. For use in Training Schools for Attendants and Nurses and in Medical Classes, and as a Ready Reference for the Practitioner. Third edition. Pp. 183. Philadelphia: F. A. Davis & Co.

The entire book bears evidence of being from a man who has a practical knowledge of the treatment of the insane. It will be particularly valuable to those physicians who, with little training and no experience in the care of the insane, are called upon to treat these cases, and also to those who are required to testify in courts of law as to mental capacity, etc. To the latter it will be especially valuable because the simple wording of the text and clear definitions of the various forms of insanity should be readily intelligible to a jury. The subject of the medical treatment of insanity is fully dealt with, though, as is proper, especial emphasis is laid on good nursing. A special chapter devoted to the nursing of the insane would also give valuable information to those who have the care of those borderline cases known as "nervous," "cranks," etc. Numerous anecdotes enliven the book and illustrate special points. C. D. C.

RECENT ADVANCES IN THE PHYSIOLOGY OF DIGESTION. By E. H. STARLING, M.D. Chicago: W. T. Keener & Co., 1906.

This exposition of so ever-changing and so recently revolutionized a subject as the Physiology of Digestion should be welcomed by every physician, whether practitioner or laboratory man, who wishes to keep abreast of advanced thought.

E. H. Starling, the author, is widely known as the co-discoverer with Bayliss of secretin, the excitor of pancreatic activity, and he can speak with a voice of just authority on questions of digestion. That a leader in a particular field of thought should himself undertake to epitomize impartially the recent work of himself and others in that line is somewhat unusual, and by such an epitomy the medical public is distinctly the gainer.

Starling begins with a consideration of the fundamentals of good metabolism, and follows this with a longer discussion on the physics of ferment action. This latter will, perhaps, be of least interest to the general reader, but it is particularly Starling's own field of work, and an understanding of it is the *sine qua non* to a grasp of the subject.

He discusses in order the secretions of the mouth, stomach, pancreas, liver, and intestines, with the pros and cons of experimental evidence; insomuch of which he has himself pointed the way. The microscopic changes in the pancreas during activity are considered at some length and the work of Cannon in this country on the movements of the intestines is emphasized and quoted.

It is hard to review, other than favorably, such a lucid attempt to diffuse knowledge of an intricate subject, and if it be considered that a somewhat laborious and time-consuming review of current literature would fail to elicit some of the material presented, much less give it the master's interpretation, the utility of the book becomes clear. The style is simple and easy. Such an "error" as occurs on page 140 in the description under Fig. 12, where "each" is followed by "are segmented" is evidently typographical. There can be no doubt that this small book is among the most notable and valuable publications of its kind. R. P.

UNIVERSITY OF PENNSYLVANIA
DEPARTMENT OF MEDICINE

FOUNDED IN 1765

This Medical School, the oldest in the United States, was founded in 1765 by Dr. John Morgan, who filled in it the first medical professorship created in America. In his opening "Discourse upon the Institution of Medical Schools in America," delivered in the College of Philadelphia May 30, 1765, Dr. Morgan uttered these prophetic words: "Perhaps this medical institution, the first of its kind in America, though small in its beginning, may receive a constant increase of strength, and annually exert new vigor. It may collect a number of young persons, of more than ordinary abilities, and so improve their knowledge as to spread its reputation to distant parts. By sending these abroad duly qualified, or by exciting an emulation amongst men of parts and literature, it may give birth to other useful institutions of a similar nature, or occasional rise, by its example, to numerous societies of different kinds, calculated to spread the light of knowledge through the whole American continent, wherever inhabited."

Through Dr. Morgan, the pupil of Hunter in London and of Cullen in Edinburgh, the graduates of this school take a just pride in regarding it as the lineal descendant of the best medical schools of Great Britain in the last century. To Dr. Morgan was soon joined another pupil of Cullen, Dr. William Shippen, as Professor of Anatomy and Surgery, thus forming another tie of relationship to the celebrated University of Edinburgh, whose methods of instruction were substantially adopted here. In the next year Dr. Adam Kuhn was added as Professor of Botany and Materia Medica; and in June, 1768, a "Commencement was held," at which medical honors were bestowed, the first in point of time in America. In 1769, Dr. Benjamin Rush was elected Professor of Chemistry, while Dr. Thomas Bond, one of the trustees of the College of Philadelphia, delivered lectures on Clinical Medicine in the Pennsylvania Hospital.

To the faculty thus composed of Morgan, Shippen, Bond, Kuhn, and Rush, have succeeded, at various times, professors whose reputation has been national, such as Wistar, Barton, Physick, Chapman, Hare, Gibson, Horner, Dewees, Jackson, George B. Wood, Hodge, James B. Rogers Carson, R. E. Rogers, Leidy, Henry H. Smith, Pepper, Francis Gurney Smith, Stillé, D. Hayes Agnew, Goodell, W. Pepper, Jr., and Ashhurst.

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Diplomas of public high schools may be accepted as complete or partial certificates. All diplomas presented by candidates will be referred to Faculty Committee No. 1 of the College Faculty (Academic), who will examine each case and decide whether the diplomas shall be accepted in lieu of examinations, and what subjects they properly cover. The diploma must be transmitted to the Dean of the Medical Faculty not later than June 10 or September 10 in each year, and must be accompanied by a certificate signed by the principal of the school, stating the exact amount of each subject covered by the diploma, and the mark or grade attained in each subject.

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UNIVERSITY OF PENNSYLVANIA MEDICAL BULLETIN.

OPSONINS AND VACCINES AS APPLIED TO SURGICAL THERAPY.[1]

By D. H. Bergey, M.D.,
Assistant Professor of Bacteriology, University of Pennsylvania.

The phagocytic power of the leukocytes was discovered by Leber (1888), but its great importance in overcoming infection was made apparent through the researches of Metchnikoff (1892). On the basis of the phagocytic power of the leukocytes Metchnikoff formulated his theory of immunity which has ever since stood in opposition to the more generally accepted theories, promulgated in Germany and elsewhere, in which the influence of the phagocytes is overshadowed by the destructive powers of the fluid portion of blood serum.

It was not until the discovery of the opsonins by Wright and Douglas (1902) and their demonstration of the important relation of these substances in the blood to the phagocytic power of the leukocytes that the full significance of this leukocytic function was comprehended by scientific investigators.

Though Metchnikoff and those adhering to the French school had for a long time proclaimed what appeared to be extravagant claims for the activity of the leukocytes in overcoming disease, notwithstanding the very generally accepted functions of forces evidently originating and existing outside the leukocytes, the discovery of the opsonins by Wright and Douglas attracted renewed attention to the teaching of Metchnikoff. While the French school regarded the increased phagocytic powers of the leukocytes in immune animals over those exhibited in normal animals, as being due to a direct stimulation of the phagocytic powers of the leukocyte through an immune substance, Wright and Douglas demonstrated that in reality the immune substances—the opsonins—acted upon the bacteria and prepared them for phagocytosis. The studies of Neufeld and Rimpau (1904) confirmed the opinion of Wright and Douglas that the immune substances—the bacteriotropins, as they called them—exerted their action upon the bacteria and not upon the leukocytes.

Our studies of both natural and acquired immunity have revealed to us several varieties of antibodies or immune substances in the blood in different diseases. The principal antibodies through which disease is prevented or overcome after it has become established are the antitoxins, the agglutinins, the precipitins, the bactericidal amboceptors, and the opsonins.

The antitoxins are the most important weapons of defence which the body employs against bacterial infection in those diseases in which the causative agents have the property of secreting soluble toxins, viz., diphtheria and tetanus. The organisms causing these diseases secrete a soluble toxin by means of which they induce the constitutional symptoms and organic lesions which characterize the diseases which they produce. Diphtheria and tetanus are the only diseases of human beings against which we possess efficient antitoxic sera as protective and therapeutic agents.

In another group of diseases, such as typhoid fever, dysentery, and Asiatic cholera, we are dealing with bacteria which do not generate soluble toxins in large amounts, but which have their poisons in intimate association with their body proteids. In immunity from these diseases the most prominent antibody is the bactericidal amboceptor, which has the power of uniting with the bacteria with one of its haptophore groups, while the other haptophore group unites with the complement of the blood and thus makes the destruction of the bacteria possible. These diseases are also characterized by the high agglutinating power of the blood serum upon the invading bacteria, a function which no doubt is of great importance in overcoming the infection.

In still another group of diseases we find that the blood serum acquires neither a high antitoxic, bactericidal, or agglutinating power, but that in these infections the opsonins are the most important antibodies that have thus far been discovered. The diseases which appear to belong to this class are those due to the streptococci, staphylococci, pneumococci, and bacterium tuberculosis in particular, while Malta fever, plague, gonorrhea, cerebrospinal fever, and anthrax are all of a similar character in respect to the immunity which results through recovery from the particular disease. The bacteria causing these diseases also produce poisons which are in intimate association with their own protoplasm, that is, endotoxins.

Opsonins capable of acting upon a great variety of bacteria are found in normal blood of human beings and the domestic animals. Whether these normal opsonins are different for each organism, or whether they possess a character which permits the opsonin to act upon any type of organism, cannot be stated at present. We know that the agglutinins found in normal blood are principally of the nature of common agglutinins, while those resulting from recovery from infec-

[1] Abstract of a lecture delivered before the graduate students of the Department of Medicine, University of Pennsylvania, June 14, 1907

tion are, in a large part, specific for the particular organism causing the infection. It is probable that in some respects the opsonins, normal and immune respectively, bear a similar relation to the bacteria.

The opsonic power of the blood is increased naturally as the result of recovery from infection, and it can also be increased by systematic immunization by means of living attenuated bacteria, by dead bacteria, or by means of certain proteid constituents of the bacterial protoplasm. Since Wright has published his important discoveries the dead bacteria are now commonly employed for this purpose.

It has become customary to speak of the suspensions of the attenuated or dead bacteria as "bacterial vaccines," since this term was employed long since by Pasteur to designate his attentuated cultures employed in the protective inoculations against different bacterial diseases. Although the word vaccine is derived from "vacca," a cow, and was first used to designate the material employed to protect against smallpox, the long-established custom of calling the bacterial suspension vaccines has given the term some degree of fixity, besides which it is not altogether inappropriate to call all of the substances used for the purpose of active immunization or protection against disease by the same name.

The results of the inoculation of the bacterial vaccines are determined by noting their effect upon the opsonic index of the blood serum of the vaccinated individual. By the opsonic index is meant the relative influence of a patient's blood upon the phagocytosis as compared with that of normal individuals.

The opsonic index of an individual's blood serum is determined by mixing in a capillary tube equal parts of the individual's serum, a suspension of leukocytes, and an emulsion of the bacteria against which the index is to be ascertained. At the same time several control tests are made with the same leukocytes and bacterial emulsion and the blood serum of several normal individuals. These several mixtures of leukocytes, bacteria, and serum are then incubated at the body temperature for fifteen minutes and then thin smears are prepared on clean microscopic slides. These smears are dried and stained, when the number of bacteria taken up by 75 to 100 leukocytes in each preparation is enumerated. If, for instance, the average number of bacteria taken up by the leukocytes under the influence of the normal serum is 20, and the average number taken up by the leukocytes under the influence of the patient's serum is 10, then, regarding the index of the normal individual as unity, the index of the patient's blood would be 0.5.

A low opsonic index is regarded as indicating an unusually low degree of resistance against infection or the presence of infection. On the other hand, a high opsonic index is regarded as indicating either a high degree of resistance to infection, probably as the result of recovery from infection by the particular organism, or a low grade of infection in which there is insufficient opportunity for auto-immunization to completely overcome the infection.

Some American investigators have expressed considerable doubt as to the reliability of the opsonic index as an indicator of the progress of infection, because of the variability of the results they have obtained in the study of the index of normal individuals as well as in the study of the effects of inoculations. Other investigators have not encountered such marked variations in their results, and hence they are inclined to agree with Wright and his associates that, while absolutely concordant results are not to be expected, nevertheless, the results of control tests should not vary more than about 10 per cent. It is well known that some of the investigators who have reported varying results have deviated from some of the details of Wright's technique, and it is probable that in this fact lies the chief cause for the nature of the results they have obtained.

The bacterial vaccines are prepared by cultivating the organisms on the surface of agar-agar and then flushing the bacteria off by means of normal salt solution. These suspensions of the bacteria are subjected to heat—65° to 80° C. for an hour—so as to kill the organisms. Inasmuch as the size of the dose inoculated has an important influence upon the patient and the course of the infection, it becomes necessary to ascertain the number of bacteria in a certain volume of the suspension. This is done by mixing equal quantities of blood and bacteria, and then by counting both erythrocytes and the bacteria in the same number of squares of a blood-counting cell the number of bacteria per cubic centimeter of emulsion can be calculated.

The size of the dose of bacterial emulsion to be inoculated must be governed by the patient's initial opsonic index, the extent of the infection, and also by the general condition of the patient, especially with regard to the presence or absence of fever. In persons with fever the dose should always be smaller than in those without fever. The interspacing of the doses is likewise determined by observing the patient's opsonic index. Immediately following an injection of the vaccine the index falls for a time—the so-called negative phase of Wright—to be followed in a day or two by a rise in the index to, or above, its original level—the positive phase of Wright. Subsequent inoculations should not be made until the opsonic index has returned to, or above, the initial point.

The extent and duration of the negative phase is influenced to a large degree by the relative size of the dose administered, that is, the larger the dose given the greater is the negative phase, and the more slowly does it give way to the positive phase. Wright directs, however, that in cases where the positive phase is slow in manifesting itself and is not pro-

nounced, it is best not to wait too long before repeating the injection, but under the circumstances he advises the administration of a smaller dose than was given at the first injection.

Wherever it is possible to do so, Wright recommends the use of autogenous cultures in the preparation of the bacterial vaccines in preference to the use of stock cultures. In the treatment of tuberculosis Wright employs Koch's new tuberculin, using 0.004 to 0.06 mgm. of the dry powder at a dose. The number of bacteria to be administered in the treatment of the other bacterial infections ranges from 50,000,000 to 500,000,000, according to circumstances. On general principles it is advisable to begin with the smaller dose and gradually increase the amount injected if the response obtained warrants such a course.

The bacterial vaccines are employed in public health work and in general medicine either as protective agents or as curative agents, and they may be employed by the surgeon on the same broad scope. While the use of the vaccines is of greatest importance to the surgeon in the treatment of certain chronic infections, where operative procedures have proven more or less disappointing, they may also be used to fortify the system against bacterial invasion in, or following, operations where aseptic and antiseptic measures cannot be satisfactorily employed.

The diseases amenable to treatment with the bacterial vaccines are: Furunculosis, carbunculosis, and circumscribed suppurating inflammations due to the staphylococci; chronic inflammations due to streptococci or pneumococci; but especially localized infections due to bacterium tuberculosis, as tuberculous lesions of the skin and bones, tuberculous glands, tuberculous peritonitis, and tuberculosis of the genito-urinary tract. In chronic tuberculous lesions, as in cases of psoas abscess, Gray (1906) directs the evacuation of the caseous material, and then follows this with injections of mixed vaccines consisting of tuberculin and staphylococcus and streptococcus vaccines. In caseous or calcareous lymphatic glands Gray follows the same procedure with gratifying results. In tuberculous lesions where mixed staphylococcus and streptococcus infection does not exist the tuberculin alone suffices to bring about a rapid reduction in the size of the infected glands, or the arrest of the infectious process.

In the treatment of various infectious processes by means of bacterial vaccines the use of certain subsidiary measures is frequently advisable to assist the body in overcoming the infection. Massage may be employed with great benefit during the time the patient is being treated with the vaccines in order to facilitate the more active penetration of the infected area by the blood and lymph carrying the specific opsonin or in reëstablishing the flow of blood and lymph through the part. Measures to induce passive hyperemia of the infected area bring about similar results. Wright has been able to demonstrate that these subsidiary measures may prove positively harmful in the absence of treatment with the vaccines because of the sudden liberation of large quantities of poisonous substances lodging in the infected area.

The bacterial vaccines may also be employed as protective agents in surgical practice where it is evident that satisfactory aseptic and antiseptic measures cannot be instituted, or in cases where the general vitality of the patient is low and it is probable that secondary infection by the pyogenic bacteria will follow.

In operations in the mouth, as for cleft palate, where it is impossible to control secondary infection by the pyogenic organisms, it is advisable to fortify the patient's system by bacterial inoculations so as to increase his opsonic index for staphylococci and streptococci before undertaking the operation.

In diabetics and albuminuries where the general vitality of the body is low it is believed that the success of surgical procedures can be materially enhanced by first raising the individual's opsonic index for the common pyogenic organisms. In a similar way secondary infection of tuberculous abscesses may be avoided, if a course of treatment with bacterial vaccines precedes the opening of the abscess.

In some accident wounds where perfect asepsis is doubtful, and where the mutilation of the tissues makes secondary infection by the pyogenic organisms probable, the use of the vaccines appears to be clearly indicated.

In conclusion, no better advice can be given than is contained in a recent paper by Wright (*Lancet*, December 2, 1905): "It is a matter of great moment, especially in immunization against tubercle, to employ in every case the smallest doses which will elicit a satisfactory response, to repeat the dose only when the effect of the preceding inoculation is passing off, and to increase the dose only when it becomes clear that the dose previously employed is ceasing to evoke a sufficient immunizing response."

COPPER IN HUMAN LIVER.

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The finding of copper in the liver tissue is so universal that it is considered by many to be a normal and not an accidental constitutent of the liver. As in the analytical work for the destruction of the tissue and separation of the metal, laboratory utensils, particularly a water bath, made of copper are employed, there is a possibility that the copper detected in the tissue may have been derived from small scales of cupric oxide which may have peeled off the water bath or brass Bunsen burner and been carried by the hot gases from the flame of the burner upward and dropped into the vessel containing the tissue.

The finding of copper in the tissues of man and of the lower animals, and in plants, is well known. As early as 1832 Sarzeau[1] found it in the flesh of the ox in the proportion of 1 mgm. in 1 kgm. of the flesh. In 1838 Devergie and Hervey[2] detected it in the tissues of a man and of a newly born child. Subsequently, Devergie found 30 mgm. of copper in the intestinal canal of a child aged fourteen years and 60 to 70 mgm. in the intestines of adult females. In 1848 Deschamp detected it qualitatively in human blood, and Millon[3] found that it was present to the extent of from 0.5 to 2.5 mgm. in 100 grams of the ash of human blood. Millon's work was confirmed by Bechamp in a laboratory in which copper gas-burners were not employed. Gautier,[4] from the results of his investigations, was of the opinion that copper was an almost constant constitutent of normal human blood and liver.

Raoult and Breton found copper to the extent of 5 mgm. per kgm. of human liver, and L'Hote and Bergeron[5] in the examination of fourteen livers from adults found from 0.7 to 3 mgm. of copper in each entire liver. The conclusion that copper was a normal constituent of the human body was opposed by Flandin and Danger, and by Tardieu and Roussin.[6]

The source of the copper in the animal organism is attributed to vegetable and animal food-stuffs. Meisner[7] in 1817 established the existence of copper in a great number of vegetables, and in 1831 and 1832 Sarzeau[8] confirmed these observations. Sarzeau, in his investigations, examined over two hundred vegetables and found copper present in every one. According to Sarzeau the proportion of copper in the plant is not so much dependent upon the nature of the soil as upon the special plant. As against this, Chevreul, in 1833, found copper in 300 grams of wheat from one locality and absent in 500 grams of wheat from another locality, and Boutinguy d'Evereux determined that copper was present in wheat grown in a soil containing copper and absent in wheat grown in a soil free from copper. Ulex[1] examined various animal tissues and detected copper in all of them. In 300 c.c. of urine from a healthy man, in 90 grams of fresh human feces, in the yolk of egg, and in 50 grams of flesh from a woman who had died a sudden death he found copper. In the muscular tissue of the horse and the ox, in Liebig's meat extract, and in thoroughly cooked beef he also found copper. The metal was also found in birds, fish, crustaceans, insects, spiders, mollusks, and in the tissues of a number of other members of the animal kingdom. He further found copper in the ash of 10 grams of a certain make of Swedish filter paper.

The interesting results obtained by Ulex induced Lossen[2] to repeat the work of Ulex, with the result that he was able to detect copper in tissues when copper-containing utensils, such as a Bunsen burner and brass supports, were used in the analytic work, but when glass utensils were substituted copper could not be detected. Thus in the cases of 125 grams of beef and in yolk of egg he was able to detect copper when a brass support and a brass Bunsen burner were used, but was unable to detect it in these substances when glass apparatus was substituted. Lossen's conclusion was that Ulex's belief in the wide distribution of copper in the animal and vegetable kingdoms is not beyond doubt. Notwithstanding Lossen's results the literature since his time contains the work of many investigations which demonstrate that copper is widely distributed in animal and vegetable tissues. Kraemer[3] has assembled a vast collection of results positive as to the finding of copper in animal and vegetable tissues. For example, the range of the quantity of metallic copper expressed in milligrams in 1 kgm. of material shown in the data collected by Kraemer is, in the case of the liver of the ox, from 8.8 to 58.85 mgm. and in the liver of the

[1] Journ. de pharm., t. xviii, p. 654.
[2] Bull. de thérap., t. xv, p. 260.
[3] Journ. de pharm. et de chim., 3e série, t. xiii, p. 86.
[4] Annal. d'hygiene publique, 3e série, No. 1, p. 21 (1879).
[5] Comptes-rendus, t. lxxv, p. 270.
[6] Etude medico-légale sur l'empoisonment, 2e ed., Paris, 1875.
[7] Journ. de Schweigger, t. xvii, p. 340 and 436.
[8] Journ. de pharm., t. xviii, p. 249, and t. xvi, p. 507.

[1] Journ. f. prakt. Chem., Band xxxv, p. 367 (1866).
[2] Ibidem, Band xcvi, p. 160, and Band xcvii, p. 512.
[3] Amer. Journ. of Pharm., June, 1905, p. 276.

sheep from 6.4 to 33.6 mgm., and in wheat from 190 to 800 mgm.

The principal purpose of the investigation here detailed was to examine into the influence of the use, in the analytical operations, of copper-containing utensils on the finding of copper in human liver.

Four methods for the destruction of the organic matter were employed:

1. The wet method of Fresenius-Babo.

The final hydrochloric acid solution which was evaporated to a small volume was treated with washed hydrogen sulphide and the resulting precipitate was collected on a copper-free filter paper; then dried and the dried precipitate was placed in a platinum crucible. The filter was incinerated and the ash was collected in the crucible. A few drops of concentrated sulphuric acid was added and an equal volume of water and a small quantity of concentrated nitric acid. The crucible was gradually heated on an iron plate and the excess of acid driven off. Finally the closed crucible was strongly heated over a Bunsen burner and the copper was weighed as cupric oxide. All of the chemicals employed were free from copper. A scraped and sandpapered iron stand upon which was placed a piece of asbestos cloth and upon the latter a porcelain water bath was used. The Bunsen burner was entirely of porcelain and the gas cocks in the fume chamber were freshly painted with asphalt varnish, and the gas was conducted through two glass towers containing absorbent cotton. The fume chamber had been thoroughly cleaned by being scrubbed with soap and water. During the progress of the work no copper utensils were used in the room in which the work was being conducted.

2. Drying the tissue in a vacuum apparatus and incinerating the dry residue in a porcelain dish over a naked flame.

The liver was cut in small pieces and evaporated to dryness in a vacuum apparatus. The parts of the apparatus with which the liver came in contact consisted entirely of porcelain and glass. The dry residue was pulverized in a porcelain mortar and then incinerated over a naked flame. The Bunsen burner employed consisted wholly of porcelain and the supports for the dish were of iron. The ash was then boiled repeatedly with separate portions of nitric acid. The nitric acid was expelled by heating with sulphuric acid and the excess of the latter acid was driven off by heat. The residue was heated with water acidulated with sulphuric acid and filtered. Washed hydrogen sulphide was conducted through the filtrate. The precipitate produced was filtered off and washed with water containing hydrogen sulphide and then dissolved in dilute nitric acid. The liquid was then diluted with water and dilute ammonium hydroxide added to make the volume 50 c.c. The blue coloration produced was compared with the color of an ammoniacal solution of copper of known strength to determine the copper quantitatively.

3. This method was the same as method 2, except that the incineration was accomplished in a muffle furnace instead of over the naked flame. The muffle employed was a new one which had not been used in any other operation.

4. Method of Neumann.

The liver in small pieces was dried in a vacuum apparatus consisting of porcelain and glass. To each gram of dried residue 15 c.c. of a mixture of nitric and sulphuric acids in the proportion of 1 volume of nitric acid to 1 volume of sulphuric acid was added. The proportion of nitric acid to that of sulphuric acid was increased as the process of decomposition progressed. This method proved to be very efficient when working with small quantities of organic material, but very time consuming when large quantities of organic material were employed.

In every case the identity of the precipitate as being copper was established by qualitative tests.

A. Liver. Negro male, aged twenty-two years. 200 grams of the moist liver were decomposed by the Fresenius-Babo method in a porcelain dish on a porcelain bath heated by means of a porcelain Bunsen burner. The copper was weighed as cupric oxide, and the amount obtained was equivalent to 0.0024 gram metallic copper.

B. Liver. From same individual mentioned in A. 200 grams of the moist liver were decomposed by the Fresenius-Babo method in a porcelain dish on a copper water bath heated by means of a brass Bunsen burner. The copper was weighed as cupric oxide, and the amount obtained was equivalent to 0.0028 gram metallic copper. The use of copper utensils evidently had little effect in increasing the amount of copper beyond that found in the same quantity of liver decomposed in the absence of copper utensils. The difference of 0.0004 may reasonably be attributed to experimental error.

A. Liver. White male, aged forty-five years. 175 grams of the moist liver were decomposed by the Fresenius-Babo method in a porcelain dish and employing a porcelain water bath and porcelain Bunsen burner. The copper was weighed as cupric oxide and the amount obtained was equivalent to 0.0037 gram metallic copper.

B. Liver. From same individual as mentioned in A. 175 grams of the moist liver were decomposed by the Fresenius-Babo method in a porcelain dish on a copper water bath heated by means of a brass Bunsen burner. The copper was weighed as cupric oxide and the amount obtained was equivalent to 0.0071 gram metallic copper. The difference in this case between the amount of copper found when copper utensils were employed and that found when porcelain utensils

were used is 0.0034 gram. The portions of liver used were cut from different portions of the liver, and consequently the increase may not only be attributed to copper from the utensils, but also copper which possibly may have been deposited in larger quantity in the locality from which one of the pieces of liver had been cut.

A. Liver. White female, aged thirty-three years. 240 grams of the moist liver were decomposed by the Fresenius-Babo method in a porcelain dish on a porcelain water bath heated with a porcelain Bunsen burner. The copper was weighed as cupric oxide and the amount obtained was equivalent to 0.0011 gram metallic copper.

A. Liver. White female, aged forty years. 69.5 grams of the moist liver were decomposed by the Fresenius-Babo method in a porcelain dish on a porcelain water bath heated by a porcelain Bunsen burner. The copper was searched for colorimetrically with the use of ammonium hydroxide. No blue coloration resulted. The ammoniacal liquid was passed through a small pledget of absorbent cotton, whereupon the cotton was colored pale greenish-blue. The colored cotton was treated with acetic acid, and the solution was tested for copper with potassium ferrocyanide with a positive result. The quantity of liver operated upon in this case was considerably smaller than in the previously mentioned cases and thus only an undeterminable amount was detected. Experiments have demonstrated to me that the limit of delicacy of the colorimetric test for copper with ammonium hydroxide is 0.0005 gram of metallic copper in 50 c.c. of solution.

B. Liver from the same individual mentioned in A. 69.5 grams of the moist liver were dried and incinerated as described in method 2. By the colorimetric test 0.005 gram of metallic copper was found.

A. Liver. White male, aged thirty-five years. 48 grams of the moist liver were decomposed by the Fresenius-Babo method in a porcelain dish on a porcelain water bath heated by a porcelain Bunsen burner. The liquid was treated with ammonium hydroxide without the production of a blue color, consequently if copper were present it must have been in quantity less than 0.0005 gram. On acidifying the liquid with acetic acid and adding a few drops of potassium ferrocyanide a chocolate-brown coloration was developed, showing the presence of a minute quantity of copper.

B. Liver. From the same individual mentioned in A. 48 grams of the moist liver were dried and incinerated as in method 2. The final liquid when tested colorimetrically with ammonium hydroxide showed the presence of 0.005 gram metallic copper.

A. Liver. Male, negro, aged thirty years. 500 grams of the moist liver were dried and incinerated as described in method 3, using porcelain and glass utensils throughout the process. The final fluid tested colorimetrically with ammonium hydroxide yielded a color corresponding to 0.001 gram metallic copper.

B. Liver. From the same individual mentioned in A. 62 grams of the moist liver were examined by method 4 (Neumann) and the resulting fluid tested colorimetrically with ammonium hydroxide yielded a color corresponding to 0.0015 gram metallic copper.

A. Liver. Male, negro, aged thirty years. 400 grams of the moist liver were dried and incinerated as described in method 3, using porcelain and glass utensils throughout the process. The final liquid tested colorimetrically with ammonium hydroxide yielded a color corresponding to 0.0005 gram metallic copper.

A. Liver. Male, negro, aged twenty-two years. 500 grams of moist liver were dried and incinerated as described in method 3, using porcelain and glass utensils throughout the process. The final liquid tested colorimetrically with ammonium hydroxide yielded a color corresponding to 0.0005 gram metallic copper.

A. Liver. Male, white, aged fifty-five years. 380 grams of the moist liver were dried and incinerated as described in method 3, using porcelain and glass utensils throughout the process. The final fluid tested colorimetrically with ammonium hydroxide yielded a blue color corresponding to 0.0005 gram metallic copper.

Finally, the incineration method was tested to determine whether any copper was lost in the process. For this purpose a solution containing cupric sulphate equivalent to 0.0881 gram metallic copper was added to 287 grams of liver cut in fine pieces and incinerated in the same porcelain dish and the ash examined according to method 2. The quantity of copper recovered, calculated as metal, was 0.073 gram. Consequently, it is probable that the results obtained by the incineration method in this investigation do not represent the quantity of copper originally present in the amount of liver employed.

A. Liver. Male, negro, stillborn child. 65.75 grams of the moist liver were decomposed by the Fresenius-Babo method in a porcelain dish on a porcelain water bath heated by a porcelain Bunsen burner. The final liquid tested colorimetrically with ammonium hydroxide yielded no blue coloration, but on acidifying the liquid with acetic acid and adding potassium ferrocyanide a chocolate-brown coloration was produced. The quantity of copper present must have been less than 0.0005 gram.

B. Liver. From same stillborn child mentioned in A. 67.5 grams of the moist liver were decomposed by the

Fresenius-Babo method in a porcelain dish on a porcelain water bath heated by a porcelain Bunsen burner. The final liquid when tested colorimetrically with ammonium hydroxide yielded a color corresponding to 0.003 gram metallic copper.

A. Liver. Male, stillborn child. 91 grams of the moist liver were decomposed by the Fresenius-Babo method using porcelain utensils as above described. The final liquid tested colorimetrically with ammonium hydroxide yielded a color corresponding to 0.002 gram metallic copper.

A. Liver. Female, white, stillborn child. 115 grams of the moist liver were decomposed by the Fresenius-Babo method, using porcelain utensils as before described. The final liquid tested colorimetrically with ammonium hydroxide yielded a color corresponding to 0.003 gram metallic copper.

A. Liver. Female, negro, stillborn child. 150 grams of the moist liver were decomposed by the Fresenius-Babo method, using porcelain utensils as before described. The final liquid tested colorimetrically with ammonium hydroxide yielded a color corresponding to 0.0015 gram metallic copper.

There is no question but that copper is a constant constituent of liver tissue. While it is a constant constituent it is by no means established that it is a normal, necessary constituent, but rather as what may be termed an accidental constituent derived from copper-containing food-stuffs. The variation in the percentage content in human liver as shown by this investigation, and the variation in content in various other tissues of the animal body and also in plant structures, as before referred to in the collection of data made by Kraemer, leads to this conclusion: When absorbed into the animal circulation it forms, according to Slowtzoff,[1] stable albumin copper salts, especially in the liver, where probably it is stored as a nucleinate of copper, and because of their stability is excreted exceedingly slowly.

Experiment number.	Race.	Sex.	Age.	Method.	Utensils.	Liver in grams.	Copper found in grams.	Per cent. copper in amt. liver employed.
1 A	Negro.	Male.	22	1	Porcelain.	200.00	0.0024	0.0012
1 B	Negro.	Male.	22	1	Copper.	200.00	0.0028	0.0018
2 A	White.	Male.	45	1	Porcelain.	175.00	0.0037	0.0021
2 B	White.	Male.	45	1	Copper.	175.00	0.0071	0.004
3	White.	Female.	33	1	Porcelain.	240.00	0.0011	0.000457
4 A	White.	Female.	40	1	Porcelain.	69.5	Trace.	
4 B	White.	Female.	40	2	Porcelain.	69.5	0.0005	0.000719
5 A	White.	Male.	35	1	Porcelain	48.00	Trace.	
5 B	White.	Male.	35	2	Porcelain.	48.00	0.0005	0.0000105
6	Negro.	Male.	30	3	Porcelain.	500.00	0.001	0.000002
7	Negro.	Male.	30	3	Porcelain.	500.00	0.0005	0.000001
8	Negro.	Male.	22	3	Porcelain.	500.00	0.0005	0.000001
9	White.	Male.	55	3	Porcelain.	380.00	0.0035	0.0000013
10 A	Negro.	Male.	Stillborn.	1	Porcelain.	65.75	0.0005	0.0000076
10 B	Negro.	Male.	Stillborn.	2	Porcelain.	65.75	0.0015	0.0000228
11	Unknown.	Female.	Stillborn.	1	Porcelain.	100.00	0.003	0.00003
12	Unknown.	Male.	Stillborn.	1	Porcelain.	91.00	0.002	0.0000219
13	White.	Female.	Stillborn.	1	Porcelain.	115.00	0.003	0.000026
14	Negro.	Female.	Stillborn.	1	Porcelain.	150.00	0.0015	0.00001

From the results noted in the first part of this article it appears that the use of the ordinary copper laboratory utensils does not constitute a source of error in the finding of copper in liver tissue.

[1] Beitr. z. chem. Physiol. u. Pathol., 1902, iii, p. 307.

A STUDY OF THE COAGULABILITY OF THE BLOOD IN DISEASE.[1]

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(From the wards of Professor John H. Musser, M.D., in the Hospital of the University of Pennsylvania.)

Professor John H. Musser suggested to me that I study the coagulability of the blood in disease, and placed at my disposal his wards at the University Hospital. Over a period of several months I examined routinely the clotting-time of the blood in all the patients admitted to Dr. Musser's service. 50 cases were examined, a total of 65 observations being made on them. While this number is entirely too small to admit of definite conclusions, it may be of some value in determining whether or not anything is to be learned from routine examination of the clotting-time.

[1] Read before the Section on Medicine of the College of Physicians of Philadelphia on March 11, 1907.

The results obtained were all practically negative and were, moreover, unsatisfactory. Each disease did not seem to have a certain definite clotting-time; the average period was about the same in the different diseases. In a given disease and even in the same patient the clotting-time varied greatly, the variations having no relation to the degree of the patient's temperature, to the character of the food or of the drugs administered, or to the time of day the observations were made, or to their relation to meal time. The results obtained by other investigators could not be confirmed.

The technique I employed was practically the improved method of Wright.[2] The apparatus consisted of eight capil-

lary tubes of equal length and caliber, and of a diameter of 0.25 mm., eight rubber caps to fit over the ends of the tubes, a rubber tube with a mouth-piece, a glass tumbler, and a thermometer. The tumbler was filled with water at blood heat and the tubes with the caps on them were placed upright in it. A ligature was applied around a finger and the tip was punctured with a spear-pointed lancet. A tube was then taken from the water, the tube and cap dried, and the latter removed. The rubber tube was attached to the capillary tube and a column of blood about 5 cm. in length was aspirated into the tube and drawn a little way up from its orifice. The tube was then replaced in the water, which was maintained at blood heat by the addition of hot water. A record was taken of the time—in minutes and seconds—at which the tube was filled. At half-minute intervals the other tubes were filled in like manner. Two minutes after the first tube was filled it was taken from the water and attached to the rubber tube, into which air was blown. If the column of blood could not be dislodged the tube was marked "clotted," a note being made of the time—again in minutes and seconds—and the next tube was immediately tested similarly. If liquid blood was expelled the tube was marked "liquid," the time being taken, and the next tube was then allowed to remain in the water half a minute longer before being tested. If clotted or clotting blood was blown out, the tube was marked "clotting," and the blood in the next tube was permitted to remain a quarter of a minute longer. The remaining tubes were tested after standing varying lengths of time until the smallest possible interval was found between a tube marked "clotted" and one marked "clotting." The time recorded with the former was taken as the coagulation time, unless the interval between the two tubes was long, when the mean was taken. Immediately after each drop was aspirated the finger was wiped dry. The ligature was alternately relaxed and tightened. Squeezing the finger was avoided as much as possible. The tubes were cleansed with water, a wire being used to break up the clot. The inside of the tube was not dried.

The unsatisfactory results I obtained seemed in a measure to be due to some fault in the technique. Without doubt there are sources of error in the examination of the clotting time, many of them known, but probably just as many or more still unrecognized. Pratt,[20] who sought to determine whether the same blood under the same external conditions, examined with the same apparatus, always showed the same coagulation-time, found the experiment very difficult to perform. The blood, after it has left the vessels, undergoes rapid and variable changes, which Pratt regarded as apparently the result of contact of the blood with the tissues. In fact, the existence in the human skin of substances that accelerate coagulation has been demonstrated by Milian.[17] Pratt[20] found the coagulation-time also affected by the part from which the blood was taken, but Murphy and Gould[18] observed no marked differences between the coagulation time of the blood drops taken from different points on the surface of the body, provided the flow had been equally free. Arthus[1] and Pratt[20] believe that the depth and extent of the cut and forcing out the blood by pressure on the tissues also affect the clotting-time. Pratt[20] noticed also that a second drop of blood obtained from a cut after the first drop has coagulated always clots more rapidly than the first, even when after the removal of the first drop the skin is cleansed carefully with water, alcohol, and ether. These last two sources of error are mentioned also by Wright,[25] who attributes them to an admixture with lymph. Wright[25] also showed the influence of lymph in decreasing the clotting time, having found the latter markedly accelerated by the admixture of fresh lymph, muscle juice, or blister fluid. Delezenne[7] showed that bird's blood from a wound clots with great rapidity in half a minute to ten minutes, but remains unclotted two to eight days if removed from the vessel with every precaution against admixture with lymph. Milian[17] says that drops in the middle of a series coagulate long after drops taken at the beginning or end. Bürker[5] and Milian[17] both showed that the external temperature had an influence on coagulability. The presence of currents of air, etc., was demonstrated by Milian[17] to affect the clotting-time, which is accelerated by anything causing evaporation and thus diminishing the quantity of water in the blood. In the hands of Murphy and Gould[18] the Wright instrument failed to give results in 15 per cent. of the observations. In a certain number of cases the blood would not coagulate at all, an occurrence that could not always be explained. Douglass[8] says that tubes must be quite dry inside when used, otherwise the coagulation appears to be diminished.

According to Buckmaster,[4] the personal equation is an important factor in the use of the Wright instrument, which requires considerable technical skill, and the results must be received with caution, unless the observer has had much practice. This writer is also satisfied that in the same man the coagulation-time on different days may, at the same temperature, vary by at least five to six minutes. Hayem[13] has shown that in the same animal on different days, or even at different times in the same day, the coagulability may vary greatly. Bürker[5] likewise states that the rate of coagulation varies during the day, the maximum, twelve minutes, being at 6 A.M.; the minimum, five to six and a half minutes, being at 2 P.M.

It often was my experience that the blood in each of the eight tubes filled from the same puncture did not always coagulate in equal periods of time. The figures I give as the clotting-time necessarily are merely approximate and represent the longest clotting-time noted in any of the tubes.

THE AVERAGE NORMAL CLOTTING-TIME.

The average clotting-time I obtained in the 65 observations I made was two minutes and twenty-four seconds, there being little variation from this.

Wright[25] gives the normal clotting-time as approximately five minutes. (Formerly he gave it as two to four minutes.) Pratt[20] found the average coagulation-time, in disease as in health, to be from four to five minutes. Vierordt[24] made 5 observations upon himself daily over a period of fifty-six days and obtained an average clotting-time of nine minutes and twenty-eight seconds. Nasse[19] gives nine minutes and five seconds as the normal for men, and seven minutes and forty seconds as the normal for women. Gendrin[10] regards ten minutes as the average, while Hewson[14] makes it three to four minutes. In his 300 to 400 observations, Douglass[8] obtained the following coagulation-times:

Group.	Average coagulability. Time in minutes.
I. Albuminuries.	
(*a*) Pregnant	5.6
(*b*) Puerperal	7.0
II. Eclampsias.	
(*a*) Pregnant	7.4
(*b*) Puerperal	7.0
III. Normal puerperal	7.3
IV. Healthy pregnant women	7.1
V. Healthy non-pregnant women	7.75

In each group the coagulability varied greatly, the shortest and the longest clotting-times in healthy non-pregnant women being five and ten minutes respectively. Murphy and Gould[18] obtained an average coagulation-time of three minutes and twelve seconds with the Brodie-Russell instrument and of four minutes and eighteen seconds with the Wright tubes.

Brodie and Russell[3] found the average clotting-time seven minutes and eight seconds. Buckmaster[4] found it six minutes and fifteen seconds; Goldhorn,[11] seven to ten minutes. Da Costa[6] gives it as two and a half to five minutes with the glass-slide method, five minutes with Milian's method, and three to six minutes with Wright's method. Bezançon and Labbé[2] obtained a normal coagulation time of ten minutes with the glass-slide method, ten to twenty minutes with the test-tube, and three to five minutes with Wright's tubes.

THE COAGULATION-TIME IN DISEASE.

Below are given the average clotting-times and the maximums and minimums I observed in each disease, together with the number of observations on which each average is based:

Disease.	*Cases.*	*Observations.*	*Average. Min.*	*Maximum. Min.*	*Minimum. Min.*
Anemia	23	28	2¾	5½	1
Aneurysm	1	1	1¾	1½	1¾
Arteriosclerosis	5	8	3	5¼	1
Ascites	3	4	2¾	3¼	1
Bronchiectasis	1	4	3½	5¼	2
Bronchitis (fibrous)	1	1	2½	2½	2½
Constipation	11	17	2½	4½	1¼
Diarrhœa	4	6	2¾	4¼	2
Encephalomyelitis (disseminated)	1	1	2¼	2¼	2¼
Endocarditis	4	4	1¾	2¼	½
Epstein-Pel disease	1	2	2	2	2
Gastritis	8	9	2	2¾	½
Intrathoracic tumor	1	1	3½	5¼	2
Myocarditis	3	2	2¼	2½	2¼
Nephritis	3	3	3½	4	2¼
Œdema	5	5	2½	4	1
Pleural effusion	6	6	1½	2½	1
Pleurisy	8	10	2	3¼	1
Pneumonia	6	12	2	2¾	1¼
Rheumatism	3	3	1½	2	1¾
Rheumatoid arthritis	2	2	1¾	2	1¾
Serositis (multiple)	1	2	3¼	3¼	3¼
Tuberculosis (pulmonary)	4	4	2¼	2¾	2
Typhoid fever	12	15	2½	1¾	1¼
Epistaxis in typhoid fever	3	4	2¼	3	2¼
Hemorrhages in typhoid fever	1	3	3¼	4¾	2¼

Both Wunderlich[26] and Lehman[15] hold that in the blood of the sick retardation of the coagulability is met with more frequently than acceleration. In my cases, however, examples of increased coagulability were very rare. As a matter of fact, my observations failed to confirm the claims of other investigators. Hassal[12] found the clotting-time increased in typhoid fever; the average time in my cases of typhoid was only two and a half minutes. Wright's claim that a condition of deficient blood coagulability usually exists when hemorrhage from the bowels occurs in this disease was in a measure borne out by my figures. In my one case the clotting-time was four and three-quarter minutes five days after a hemorrhage followed by the administration of gelatin internally, two and three-quarter minutes twelve days after the hemorrhage, and two and one-quarter minutes sixteen days after this complication. On the other hand, the average clotting-time of my cases of typhoid fever in which nose-bleed was a symptom was only two and one-quarter minutes, although Wright[25] finds deficient coagulability in cases of epistaxis. Hassal[12] and Ehrlich and Lazarus[8] state that the clotting-time of the blood is increased in chlorosis and anemia; although Wunderlich[26] says that there are many exceptions to this rule. The average clotting-time of my 28 observations in anemia was but two and one-half minutes. According to Wright,[25] the coagulability of the blood is usually found deficient in the presence of transudation of lymph or plasma (called by him "serous hemorrhages"), some œdemas, effusions into joints and serous cavities, and in serous diarrhœa. In my cases, on the contrary, the clotting time was only two and one-half minutes in ascites, two and one-half minutes in œdema, as short as one and one-half minutes in pleural effusion, and two and three-quarter

minutes in diarrhœa. Vierordt,[24] Wright,[25] and Rogers[21] found the clotting-time increased by the inhalation of carbon dioxide. Yet in my cases of pneumonia, a condition in which there is an excess of carbon dioxide in the blood, the blood coagulability was but slightly diminished, averaging two minutes. In one case of pneumonia during the height of the disease, when the temperature averaged 102.2°, the clotting-time taken on four different occasions averaged two minutes seven seconds, but during convalescence, when the temperature averaged 98.2°, the clotting-time on two tests averaged one minute twenty-two seconds. The three above-mentioned writers find the clotting-time retarded by the ingestion of alcohol. This was not my experience. Of 23 observations made on 12 patients who were taking whisky the average clotting-time was two and a half minutes, the maximum being five and three-quarter minutes, the minimum one and one-quarter minutes. Wright[25] states that in hemophilia the blood is characterized by a notable leukopenia, especially polynuclear. Stessano and Billon[23] have shown that the amount of the blood in the fibrin ferment is in proportion to its richness in leukocytes. Stessano,[22] moreover, believes that the different kinds of leukocytes play a part in the coagulation of the blood and elaborates a hypothesis that the mononuclears are more particularly concerned in setting free the fibrin ferment. This led me to investigate if there was any connection, as a rule, between the clotting-time of the blood and the number of leukocytes. In 33 cases (excluding those of pneumonia) in which the clotting-time was two and a half minutes or longer the leukocytes averaged 8671. (Adding 2 cases of pneumonia brings the average up to 8994.) In 43 cases (excluding pneumonia) in which the clotting-time was less than two minutes the leukocytes averaged 8176 (adding 15 cases of pneumonia brings the average up to 14,017). In the aforementioned case of pneumonia during the first three examinations made when the leukocytes averaged 50,653, the clotting-time averaged two minutes ten seconds; during the last three examinations when the leukocytes averaged 9286, the clotting-time averaged one minute and thirty-five seconds. The results of Vierordt's[24] investigation of the blood coagulability in diseased conditions was rather indefinite and unsatisfactory. The same may be said of my own. Nevertheless it is possible that something may be learned from a routine examination for the coagulability of the blood. With a method less liable to errors in technique than that with Wright's tubes, such an examination necessarily would be of more practical value.

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AN IMPROVED METHOD OF STAINING FIBROGLIA, MYOGLIA, MYOFIBRILLE OF STRIPED MUSCLE, ETC.

By Arthur F. Coca, M.D.

In an earlier communication attention has been called to the fact that it is possible, by means of a slight modification of Borrel's magenta-picro-indigo-carmine method, to stain the intracellular fibrils of striped and unstriped muscle cells and those of embryonal connective-tissue cells. While the method as given did, when successfully carried out, offer certain advantages it could not be recommended as a reliable means for the demonstration of the fibers; for the magenta was so loosely bound—and this disadvantage applies also to its union with the cell nuclei—that only seldom, even after very rapid passage through the high alcohols, could good preparations be obtained. Another great drawback to Borrel's procedure is that it is almost impossible to secure an even differentiation throughout the entire section, while the staining of several sections on one slide fails entirely.

The modification which is now offered removes completely the disadvantages mentioned, inasmuch as the sections may be left in alcohol several minutes without any danger of over-extraction of the magenta. The stain is quickly washed out of all structures excepting the nuclei, the fibrils mentioned, bacteria, fibrin, and, in addition, fibrils which, by the methods previously given, were not colored at all—the fibrils of the epidermal cells. On the other hand, these elements hold the color so firmly that the method becomes a perfectly safe one for their demonstration.

For the staining also of protozoan parasites in the tissues, for which it was originally designed, the method has been essentially improved. The steps are as follows:

1. Zenker fixation.
2. Paraffin sections at 5μ or less.
3. Removal of paraffin, etc., to 95 per cent. alcohol.
4. 95 per cent. alcohol containing 1 per cent. iodine, five to ten minutes.
5. *Directly into water without previous removal of the iodine.*
6. Concentrated aqueous solution of magentarot (Grübler), fifteen minutes.
7. Rinse in water.
8. Three to five minutes in the following: Indigo-carmine (Grübler), 0.75 grm.; saturated aqueous picric acid, 100 c.c.; distilled water, 100 c.c.
9. Differentiate in 95 per cent. alcohol one to two minutes.
10. Absolute alcohol, one minute.
11. Xylol, balsam.

BOOK REVIEWS.

The Practitioner's Library. The Practice of Obstetrics in Original Contributions. By American Authors. Edited by Reuben Peterson, A.B., M.D. Philadelphia and New York: Lea Brothers & Co., 1907.

This system of obstetrics forms a companion volume to those upon the related subjects of gynecology and pediatrics. It contains over a thousand pages, is replete with illustrations, most of which are very creditable, and it is not necessary to say that its mechanical preparation is all that could be desired. We note certain typographical errors and some evidences of careless proof-reading which will be corrected in subsequent editions. The first two chapters, contributed by G. Carl Huber, are concerned with the physiology and development of the ovum. Over eighty pages are devoted to a full consideration of the subject, and the author especially calls attention to the need of further work in this province and deplores the waste of good material in the hands of the general practitioner. He advocates that all specimens of early ova should be preserved and sent to a skilled embryologist without needless previous handling—advice with which we are in hearty accord. Walter P. Manton follows with the consideration of the physiology of pregnancy. His chapter upon the diagnosis of pregnancy is particularly good. In the chapter upon the changes incident to pregnancy he makes the statement that the taking up of the cervix is more apparent than real, a dictum with which we are not in accord, at least in primiparæ. We would question his statement that the pressure of the corset upon the uterus tends to the production of albuminuria and uremia. The same author contributes a chapter upon the physiology of pregnancy, which, while some of its recommendations and restrictions have not seemed justified in our experience, is a valuable contribution, particularly for the general practitioner.

Henry F. Lewis contributes chapters upon the phenomena and management of the puerperal period as well as the major portion of the pathology of the same interval. He also is the author of the chapters upon the newborn infant. The chapters upon artificial feeding and injuries and diseases of this period of life are particularly good. We note with disapproval his treatment of the cord by a perforating ligature and would criticise unfavorably his treatment of ophthalmia neonatorum, particularly the preference which he exhibits for protargol and argyrol in inadequate strengths instead of silver nitrate. We are also opposed to his idea that the hemorrhagic diathesis is to be ascribed to hemophilia in a conside able proportion of the cases, and we doubt the accuracy of his statement that the navel is the site of the entrance of infection in a large number of cases. His chapter upon infection in the puerperium

is very satisfactory, being full and complete in its scope and clearly expressed. The descriptions of the diagnosis and differential diagnosis of the condition are exceptionally good, though after a rather extensive experience with the bacteriological examination of the uterine lochia we cannot agree with him in his belief in the utility of this method from the standpoint of the general practitioner. This, however, may still be considered as a matter of opinion and we are greatly pleased with his exposition of the subject in general, it being one of the most concise and clear presentations of which we have knowledge. We would wish that greater emphasis had been placed upon the value of the blood examination as a means of early diagnosis in obscure cases of sepsis. The author very happily emphasizes the frequent futility of all therapy in this condition, his opening paragraph upon the subject of the treatment being worthy of careful digestion. We are glad that the value of normal saline is emphasized as particularly suitable for intrauterine douching; but we question whether it is wise to allow a parturient to be lifted upon the commode as early as the third day.

W. A. Newman Dorland is responsible for the portion of the book devoted to the consideration of labor. We consider this one of the most important divisions of the whole subject, and it gives us pleasure to congratulate the author upon the presentation of his portion of the work. He begins with a consideration of the obstetric pelvis, and follows this with chapters upon the mechanism, the clinical course of labor, the preparations for labor, its management and the fetal and maternal examination. In his chapter upon the preparation for labor he devotes a page to well-timed adverse criticism of the midwife, with which we are in entire accord. We cannot agree, however, with his advice that the patient should remain quiet in bed or chair during the first stage of labor, and we feel that he has inadvertently been a little indefinite in his limitations of the examinations needful in an ordinary labor. We are also opposed to the author's absolute dictum with regard to the impropriety of instrumental rupture of the membranes, since it is certainly often proper to rupture the membranes in primiparous women after full dilatation has been secured. The directions for the administration of anesthetics during labor are misleading, through an unfortunate choice of words, since the author cannot intend to convey the idea that in a normal case, in which the agent has simply been exhibited to produce analgesia, there need be a depressing effect from which the patient must be given time to recover before the placenta is to be expelled. We are as loath, as is the writer, to advise a hasty interference with the normal mechanism of the third stage, but we cannot admit the justification of depression by anesthesia in a normal case. It is certainly unfortunate that the advice is given to introduce the fingers for the removal of fragments of secundines from the uterine cavity, since it is surely a matter of daily experience that small portions of the membranes are spontaneously extruded, and it is bad policy to advise anything tending to encourage interference with the vaginal tract immediately after delivery.

The pathology of labor, covering eleven chapters, has been entirely contributed by John F. Moran, with the exception of one chapter, that upon pelvimetry by Ehrenfest. In general the presentation of the matter comprising this section is adequate and we are glad to congratulate the author upon his work. We feel, however, that the dictum that after an hour's hard pains any case which does not show engagement should be considered as proper for the termination of labor, had better be modified lest a worse thing befall. The incompleteness of the differential diagnosis of uterine inversion and also the paucity of the treatment recommended for premature separation of the placenta are to be deplored. The advice to rupture the membranes in the treatment of placenta previa, while certainly indicated in many cases, is not in our opinion quite the sovereign form of procedure that a perusal of this section would indicate, and we fail to understand why, in speaking of the use of bags, the Champétière de Ribes is advised solely, no mention being made of the much more satisfactory instrument of Voorhees. Compression of the aorta has been omitted from the therapeutics of postpartum bleeding, and, while the general lack of its recognition probably renders this criticism slightly unfair, its inclusion as a temporary means to check hemorrhage would have added greatly to the value of the advocated therapy. Certainly a more emphatic warning against deep anesthesia in the last stage of the expulsive period would have been in place, since it is so fruitful a cause of uterine relaxation. In the treatment of eclampsia it would have been well to insist upon the differential indication between cervical incisions and vaginal Cesarean section, and we are sure that the great majority of competent operators would prefer the latter instead of the abdominal method in dealing with a moribund eclamptic, the child being still alive; surely a most rare condition.

In considering the treatment of the minor degrees of pelvic malformations Moran follows the lead of those who do not admit the indication for the performance of premature labor shortly before term; we are at a loss to understand the views of this school and are sorry that such teaching appears in a book of this character designed for the general practitioner. In considering the influence of operations designed to restore a retrodisplaced uterus to its normal position, the author says truly that fixation should never be performed upon a woman within the possible period of child-bearing. This is undoubtedly true, but we are led to believe that under the term fixation are placed all cases in which a little of the rectus muscle has been included in the stitch. This is a common belief, but is a mistake both on historical and anatomical grounds.

We do not consider that his treatment of breech delivery is as clear as is to be desired, and we object to the implication that posterior rotation of the occiput in head last cases may be an unpreventable accident.

Hugo Ehrenfest's contribution is concerned with the general disturbances and complications of pregnancy, the premature expulsion of the ovum and pelvimetry. As an introduction to the section devoted to the pathology of the pregnant state, he gives a most satisfactory *resume* of the recent theories concerning the etiology of toxæmia, and we are delighted to see that while the importance of most careful urinary studies is insisted upon, the author does not give the importance to the estimation of urea which is ascribed to it by some recent authors. His original work in pelvimetry renders his contribution upon this subject of more than usual interest, and we are much pleased with his timely caution regarding the limitations of the deductions to be drawn from pelvic measurements. He completes his chapter, upon this subject, with a complete account of the methods of internal and external pelvimetry; a short account with the relative importance of the various measurements, and a short historical sketch of the various instruments, which have been devised from the time

of Stein to the present, with illustrations of the most important modifications.

Montgomery A. Crockett has, as his field, the consideration of the obstetric operations. In his discussion upon the preparation necessary for the performance of obstetric surgery he emphasizes forcibly the surgical nature of obstetrics as a whole. We are glad to note that he would avoid the impressive but dirty Kelly pad in his operations. We are surprised that the curettement forceps of Emmet does not receive the consideration which is certainly its due, either in the treatment of sepsis or in the chapter upon minor operative procedures. The dangers of the curette are, on the other hand, well stated. The author believes that all must agree with Williams, that the only indication for the employment of premature labor is the combination of a very large head in a normal pelvis, as previously mentioned. We quite fail to grasp the obligation to agree with him in this matter.

Contrary to the author, it has been our experience that anesthesia, preferably by ethyl chloride or chloroform, is indicated in the introduction of the bag for dilatation of the cervix. This is certainly the case in primiparous women. We are much pleased with the absolutism of the writer in regard to the use of rubber gloves in obstetrics. It is a pleasure to note that he advocates the axis-traction principle in practically all forceps operations above the outlet. There is certainly room for a difference of opinion with regard to the statement that the application of forceps, whether high or low, demands anesthesia, if by this the surgical degree is meant. The use of the axis-traction rods during the delivery of the head over the perineum, as shown in an illustration, is useless and cumbersome.

We fear that a man depending only upon the instructions given by Crockett, for closure of a complete tear of the perineum, would find that they were inadequate and we would suggest that in describing the operation of hebotomy the incisure should be advised upon the side toward which the occiput is directed.

Alfred S. Warthin presents chapters upon the pathology of the placenta, the deciduæ, the chorion, the amnion, the umbilical cord, the pathology of the fetus, and we take pleasure in stating that he has succeeded in making this usually dry portion of the subject of decided interest. Not only does he give attention to the scientific delineation of the subject, but he also draws interesting, practical deductions from his studies. His description of chorio-epithelioma malignum is particularly good.

Benjamin R. Schenck contributes the chapter upon extra-uterine pregnancy. It covers thirty-seven pages, and, although we cannot approve all the advice given, it is a very satisfactory work. He advocates operation in practically all cases, but takes a conservative position when considering the treatment after viability, in that he advocates waiting after the death of the child until thrombosis of the placental vessels can occur. We question decidedly the advisability of awaiting viability the diagnosis having been made shortly before that period, as we believe that the chance of a living and healthy child can not outweigh the maternal risks.

Charles S. Bacon has written a very satisfactory chapter upon the care of premature infants as well as the chapter dealing with lactation and infections of the breasts.

The contributors are to be congratulated upon the general excellence of the exposition of the various subjects allotted to them, while the editor deserves the thanks of the profession for his choice of authors and the manner in which his difficult task has been consummated. W. R. N.

Essentials of Human Physiology. By D. Noel Paton, M.D., B.Sc., F.R.C.P. Ed., Superintendent of the Research Laboratory of the Royal College of Physicians of Edinburgh; Lecturer on Physiology, School of Medicine of the Royal Colleges, Edinburgh; Examiner in Physiology in the University of Glasgow and for the Royal College of Physicians, Edinburgh; and Late Examiner in the University of Edinburgh. Second edition, revised and enlarged. Chicago: W. T. Keener & Co. Edinburgh and London: William Green & Sons, 1905.

The physiology of the human being, by Paton, possesses the same briefness and clearness of description as the author's former work in veterinary physiology. The book is probably not comprehensive enough to meet all the demands of the medical student, nor does it possess qualities which instil enthusiasm in the reader, yet it serves a useful purpose in several ways. In the first place, it is a valuable book to be used by the busy doctor, who quickly wishes to learn a physiological fact; secondly, it is the kind of book which is useful in "brushing up" for examinations; and, thirdly, if one desires to have a general idea of a subject before studying its details the work will be found to serve this purpose very well. This last point is demonstrated in the chapter on Internal Secretions. The work in this field is very voluminous, so much so that many very important and fundamental facts are buried by details. The author has here demonstrated his power of selecting the material that is most essential to give the reader a good idea of the subject in general. The illustrations are modest and not elaborate, but serve the purpose of making clear many points, as well as and, in fact, even better than the more beautiful and complex illustrations seen in some other much-read text-books. The author has endeavored "to put before the medical students, as succinctly as possible, the essential facts of human physiology," and he has succeeded. E. L.

The Subconscious. By Joseph Jastrow, Professor of Psychology in the University of Wisconsin. Boston and New York: Houghton, Mifflin & Co., 1906.

It requires a considerable amount of boldness to enter the lists of that dispute which has been waged from the time of Aristotle and Plato, but to attempt to write upon "the subconscious" and present the subject for popular comprehension is heroism indeed, yet this is what Professor Joseph Jastrow has attempted. Whether he has accomplished this is a question.

The author in his preface says "that the word subconscious has a dubious sound, and those to whom it brings slight illumination associate it with questionable phenomena of rare occurrence and unusual significance. The word, in company with others of analogous origin, has been made the symbol of an inner mystery, a pale double of ourselves, disporting itself strangely when our oversight is relaxed, and

capable, if only its excursions could be followed, of overthrowing the limitations of sense and of discounting our most accredited psychological currency."

Professor Jastrow subdivides his book into three parts: He first treats of the normal subconscious; second, of the abnormal, and, lastly, he considers the theoretical. Under the first heading he attempts to elucidate the function of consciousness, its relation to volition and attention; the methods in mental procedure; the maturing of thought; the mechanism of consciousness, and its relation to the nervous system. He brings to bear a large amount of homely illustrations which are truly of wide range. Under the abnormal, he speaks of "dream consciousness," and its varieties, disassociated consciousness, and altered personality. Here he makes use of the celebrated case of Morton Prince. In his last division he considers the conception of the subconscious as an abnormal entity.

The reader, who is in the hope of having the subconscious made clearer to him, will agree with Professor Jastrow, that the subconscious is an elusive phenomenon, and cannot be well defined; at least the contents of the book leaves one's thoughts in a hazy condition. The illustrations made use of are entertaining and the story which is woven is interesting, and it is probable that the author made the subject as clear as it can be made. Certainly to write upon this subject for popular comprehension is a difficult task. The impression one gains after reading the book is that it is too deep for the purpose intended, and not good enough for the psychologist. Many criticisms could be made, especially as regards Professor Jastrow's views of the relation of the nervous system to the subconscious. On the whole, it is an interesting work, and worthy of attention. T. H. W.

Organic and Functional Nervous Diseases. By M. Allen Starr, M.D., Ph.D., LL.D., Sc.D. Second edition, thoroughly revised. New York and Philadelphia: Lea Brothers & Co., 1907.

When the first edition of this book, then limited to the discussion of organic diseases of the nervous system, appeared a few years ago, reviewers almost universally bespoke a successful future for it. This has evidently been realized, as the very early appearance of this second edition will attest. The addition of a section on functional diseases has made the book much more valuable. A number of disorders usually included in works on neurology are, however, still excluded. Thus such diseases as acromegaly, cretinism, myxedema, exophthalmic goitre; certain infectious diseases, as tetanus and hydrophobia, and the so-called trophic disorders, as lipomatosis, megalocephaly, scleroderma, and angioneurotic edema, are omitted, the author holding that they are more properly discussed in works on internal medicine, which seems to be a point well taken.

The author states in his preface that the statements presented are in a large part based upon his own large experience of twenty-five years' duration, and one of the valuable and unique features of the book is the frequent introduction, after the symptomatology of a disorder has been discussed, of clinical histories of actual cases. One of the most excellent features of the work is the therapeutics; the reviewer knows of no book on nervous diseases where the directions for treatment are so full and generally excellent. We would question, however, the use of adrenalin in cerebral hemorrhage, and wonder that cerebral decompression as now practised is not mentioned under the treatment of tumors of the brain. The condemnation of the treatment of the tic douloureux with large doses of strychnine we do not consider warranted. Among the articles which seem to the reviewer of unusual excellence may be mentioned those on epilepsy, neurasthenia, although the rest cure is not mentioned among the methods of treatment, but is later under hysteria; and multiple neuritis. In discussing paralysis agitans the author leans toward the muscular theory as the cause. The fact, true but not usually emphasized, that a general neurasthenic condition underlies the occupation neuroses and should influence the treatment is in this book impressed upon the reader. No book, however excellent, has been perfect, and among sins of omission in this are the non-mention of uremic palsies in discussing the differential diagnosis of apoplexy; the diagnosis of Friedreich's ataxia from multiple sclerosis is not given; arthritic muscular atrophy and diffuse sclerosis are not mentioned at all; hereditary chorea is dismissed with a very few lines, the author stating that he has never seen a case, which seems remarkable. The discussion of degeneration of the spinal cord due to pernicious anemia and various other exhausting and toxic conditions under the head of Combined Sclerosis on page 323, and then later on page 331 under that of Pernicious Anemia and its Effects on the Spinal Cord discussing them again, seems to be confusing.

The illustrations and diagrams, many of them original, are frequent and mostly excellent. That on page 673 hardly gives a good idea of hemiatrophy of the tongue, as it is supposed to do.

It can be truthfully said that this book is a credit to American neurology and can be commended to those in search of an exhaustive text-book on nervous diseases. G. S. P.

Syllabus of Lectures on Human Embryology. By W. P. Manton, M.D., Detroit College of Medicine. Third edition. Philadelphia: F. A. Davis Co., 1907.

This synopsis is intended primarily to accompany the author's own lectures and is interleaved with blank pages for additional notes by the student. The book itself by means of headings and short paragraphs covers a wide field, and necessarily many of the points touched on are treated very briefly. As the author states, the student needs further information through books, lectures, and practical work, for without this he would often be left in a maze. The fact that this is the third edition shows that the book is found useful to many. Some changes have been made in the text and a number of the illustrations have been changed from the second edition.

The description of methods for practical work, written when the author was an enthusiastic naturalist, has been retained in a slightly amended form and serves to give some living interest to the briefly presented subject.

W. H. F. A.

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FOUNDED IN 1765

This Medical School, the oldest in the United States, was founded in 1765 by Dr. John Morgan, who filled in it the first medical professorship created in America. In his opening "Discourse upon the Institution of Medical Schools in America," delivered in the College of Philadelphia May 30, 1765, Dr. Morgan uttered these prophetic words: "Perhaps this medical institution, the first of its kind in America, though small in its beginning, may receive a constant increase of strength, and annually exert new vigor. It may collect a number of young persons, of more than ordinary abilities, and so improve their knowledge as to spread its reputation to distant parts. By sending these abroad duly qualified, or by exciting an emulation amongst men of parts and literature, it may give birth to other useful institutions of a similar nature, or occasional rise, by its example, to numerous societies of different kinds, calculated to spread the light of knowledge through the whole American continent, wherever inhabited."

Through Dr. Morgan, the pupil of Hunter in London and of Cullen in Edinburgh, the graduates of this school take a just pride in regarding it as the lineal descendant of the best medical schools of Great Britain in the last century. To Dr. Morgan was soon joined another pupil of Cullen, Dr. William Shippen, as Professor of Anatomy and Surgery, thus forming another tie of relationship to the celebrated University of Edinburgh, whose methods of instruction were substantially adopted here. In the next year Dr. Adam Kuhn was added as Professor of Botany and Materia Medica; and in June, 1768, a "Commencement was held," at which medical honors were bestowed, the first in point of time in America. In 1769, Dr. Benjamin Rush was elected Professor of Chemistry, while Dr. Thomas Bond, one of the trustees of the College of Philadelphia, delivered lectures on Clinical Medicine in the Pennsylvania Hospital.

To the faculty thus composed of Morgan, Shippen, Bond, Kuhn, and Rush, have succeeded, at various times, professors whose reputation has been national, such as Wistar, Barton, Physick, Chapman, Hare, Gibson, Horner, Dewees, Jackson, George B. Wood, Hodge, James B. Rogers, Carson, R. E. Rogers, Leidy, Henry H. Smith, Pepper, Francis Gurney Smith, Stillé, D. Hayes Agnew, Goodell, W. Pepper, Jr., and Ashhurst.

ADMISSION.

Admission to the Department of Medicine may be obtained either: I., by diploma; or II., by examination; or in certain cases, as specified below under I., by a combination of both methods.

I. Admission by Diploma: Any candidate who may have received a degree in Arts or Science from a college recognized by this University will be admitted without examination. Candidates who may have been admitted by examination to the two-year course in Biology of this University, and who may have satisfactorily completed the course, will be exempt from the entrance examination. Any candidate who may present written evidence of having passed the entrance examinations of a recognized college, in which the requirements are equivalent to those demanded for entrance to the Freshman Class of the College (Arts and Science Courses) of this University, will be admitted without examination.

Diplomas of public high schools may be accepted as complete or partial certificates. All diplomas presented by candidates will be referred to Faculty Committee No. 1 of the College Faculty (Academic), who will examine each case and decide whether the diplomas shall be accepted in lieu of examinations, and what subjects they properly cover. The diploma must be transmitted to the Dean of the Medical Faculty not later than June 10 or September 10 in each year, and must be accompanied by a certificate signed by the principal of the school, stating the exact amount of each subject covered by the diploma, and the mark or grade attained in each subject.

II. Admission by Examination: The required subjects of examination for entrance to the Department of Medicine are the same as those prescribed for admission to the Freshman Class of the College (Arts and Science Courses) of the University of Pennsylvania.

The course of instruction extends over four years, with one session, beginning the last Friday in September and ending on the third Wednesday in June in each year.

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THE VALUE OF CHEMICAL AND BIOLOGICAL METHODS IN MEDICAL DIAGNOSIS.[1]

By Alfred Stengel, M.D.

It is impossible to present in the limits of this discussion any adequate account of the history of the relation of chemistry and the methods of biology to clinical diagnosis, and it were rash even to attempt a complete review of the relative value of chemical and biological methods as compared with the older clinical procedures. In the very beginning of my discussion I would insist that such a comparison, if undertaken in any spirit of partisanship, could not be other than harmful and unjust. In the rapid development of the more rigidly scientific methods of diagnosis emanating from the laboratory, a feeling of disregard, if not contempt, for the older clinical methods has too often made its appearance, not rarely perhaps on account of a greater familiarity of many with these newer means of investigation. In the course of my remarks I shall have occasion to indicate the varied directions in which greater accuracy of diagnosis has been attained and broader conceptions of the natural history of disease have been established through the aid of the methods of chemistry and biology, but it must not be forgotten that the original foundations of our modern medicine rest upon accurate observations of disease without the aid of these newer sciences. Furthermore, it is perhaps too commonly forgotten that the methods of laboratory investigations are subject to errors of personal equation; that they are surrounded with pitfalls for the unskilled or careless; and that their capacity for misguiding those who place implicit confidence in their results without regard to the care or skill of the individual to whom such examinations are entrusted and without the check of confirmatory clinical examination is in direct proportion to their reliability when carefully performed and their value rigidly estimated.

From time to time iconoclasts appear who decry either the clinical or the laboratory methods of diagnosis. Doubtless these serve some useful purpose, though their opinions are manifestly one-sided and born of a narrow conception of the whole problem. The broadly trained clinician can no more dispense with the newer methods than with the older and more settled processes of observation and induction. Knowledge and experience with the laboratory methods alone are quite compatible with brilliancy but not with breadth of view, and familiarity with the clinical methods only does not constitute the equipment of a modern diagnostician. A substantial general education which alone can give to the average man breadth of view and the capacity of reaching just conclusions in matters of any sort, thoroughly trained powers of observation, accurate clinical experience, and practical familiarity with the laboratory methods are the fundamentals upon which diagnostic acumen must rest. Without any one of these the product is unfinished. So far as laboratory aids are concerned, it may be well for those of a critical mind to recall that the successive steps in the knowledge of a certain disease have often been made possible largely or wholly by the help furnished from the laboratory, and that though the chemical or biological methods may afterward be unessential in studying a given case, the proper understanding of that case is none the less dependent upon the data available through such methods. It may, for example, be unnecessary to examine the sputum in some instances of pulmonary disease, but the routine application of this together with other laboratory methods enabled scientific physicians to establish more certainly the ordinary clinical distinction of allied conditions, and even in the cases cited the diagnosis would be somewhat more certain if fortified with the examination of the sputum. His is surely a myopic vision who sees cause for satisfaction in his ability to diagnosticate without laboratory aid when the clinical distinctions upon which his diagnosis rests were established by those who faithfully applied the laboratory method.

THE CONTRIBUTION OF CHEMISTRY TO DIAGNOSIS.

It is not surprising that the methods of chemical analysis were early applied to the study of physiological processes and to diagnosis; and, though we shall find abundant reason for disappointment in the results achieved, may it not be said with truth that the disappointments have been mainly evident when the flight has been too ambitious? The newer chemistry of the last few decades with its wider appreciation of the laws of physics has at least demonstrated some of the variables that were and are even now of necessity ignored in ordinary chemical methods. It is these factors in particular that will need incorporation in all new attempts to gauge organic functions by chemical methods, and without them such methods must still remain but approximative and inexact.

[1] This paper was part of a discussion on the "Historical Development and Relative Value of Laboratory and Clinical Methods in Diagnosis," held at the Congress of American Physicians and Surgeons, in May, 1907.

To the skeptic who believes that chemistry has contributed nothing to accuracy of diagnosis we need but recall that the precise diagnosis of renal disease was quite outside the range of clinical methods until Bright demonstrated the relation of coagulability of the urine to organic disease of the kidney; that the differentiation of diabetes mellitus from polyuria and from some other metabolic disturbances rests upon the chemical methods of diagnosis; that our knowledge of acid intoxication, of various blood poisonings, and of certain nutritional diseases is almost wholly dependent on the chemical study of the secreta, blood, and excreta. If we must in some cases admit some disappointment in the scope and accuracy of chemical methods in immediate or ultimate diagnosis, we must nevertheless appreciate their indirect value in casting side lights on the diagnosis of obscure conditions as well as their frequent direct value in determining variations in the course of disease.

Early Chemical Methods. The birth of modern chemistry may be said to have even date with the discovery of oxygen, and we may find, in the literature of the period immediately following, the date records of painstaking chemical studies, chiefly of the blood and pathological exudates, such as those of Andral, Denis, and other French clinicians. Lavoisier, who had named oxygen soon after its discovery, was quick to appreciate its fundamental importance in the process of life, and with La Place initiated studies of animal heat and respiration that were amplified by Liebig, Voit, Pettenkofer, Pflüger, Crawford and a long line of later chemists upon whose investigations has been based our knowledge of the science of nutrition. It was sometimes hoped that studies of the external and internal respiration might prove of direct value in practical medicine as they have proved in solving various problems in the pathogenesis of disease. Though this hope has not been realized on account of the difficulty of the methods, the practical results achieved in the laboratory form the basis of much of our modern knowledge of nutritional disease.

Another early direction of chemical study was toward the physiology of special organs. Cotugno had recognized the coagulability of the urine even before the era of modern chemistry and Bright soon afterward demonstrated the practical diagnostic value of this chemical fact in the recognition of renal disease. Spallanzani had recognized the chemical nature of digestion as early as 1793 and Prout discovered the acidity of the gastric juice in 1824. Beaumont's epochal study of the celebrated case of Alexis St. Martin was published in 1833. Not long after that date Claud Bernard began his work at the College de France and laid the foundations of our knowledge of the functions of the liver, discovered the action of the pancreatic juice, and cast the first light on the nature of diabetes mellitus.

It may be profitable now to review very briefly some of the uses of chemical methods in the practical diagnosis of disease.

Disorders of Metabolism. The early methods, as I have already stated, were concerned with the study of the respiratory exchange of gases and, though of inordinate value in determining the fate of food-stuffs and the production of heat and energy, thus establishing the science of nutrition, have proved of little direct practical value. The pathologist found these studies of interest in disproving the existence of decreased oxidation, often assumed to be present, in such diseases as anemia, gout, leukemia, and diabetes, but the practical physician has too little reflected upon their relations to clinical medicine.

Proteid Metabolism. Liebig conceived the idea that the estimation of nitrogen elimination might be useful in determining proteid metabolism and Voit demonstrated nitrogen equilibrium, the balance between the intake of nitrogen in food and the output in urine and feces. The uselessness in nutrition of the nitrogen inhaled in atmospheric air had been long before established. Not unnaturally urea as the chief end product of nitrogen metabolism and as a fairly determinable chemical body received a large share of attention, and notwithstanding fuller knowledge is still regarded by many as a valuable index of certain metabolic and excretory processes. In the light of present knowledge we recognize that increased ingestion of proteids and augmented tissue destruction may each increase the excretion of urea, while decreased ingestion, faulty absorption, and defective excretory processes may reduce its amount. The mere determination of the amount of urea excreted in the urine, without reference to the nitrogenous intake and the degree of intestinal absorption, is therefore valueless, and even when the diet is fixed and absorption accurately determined, the proportion of urea independent of total nitrogen elimination is almost equally valueless. Much supposedly scientific labor is still wasted and erroneous deductions based on this useless determination. There are undoubtedly some scientific short-cuts which enable practical men to reach useful conclusions by establishing one main factor and ignoring others that are negligibly small, but the determination of urea in the urine is not one of these. If proteid metabolism is under consideration, careful estimations of the total ingestion and total excretion and determination of the form of excretion are indispensable. Ready methods of measuring one factor cannot but lead to erroneous conclusions.

Studies of purin metabolism and the excretion of uric acid constitute a later sphere of chemical investigation. By slow processes we have learned that the uric acid of the urine has two sources: a part is derived from the nuclein of ingested food, a part from that of the tissues undergoing katabolism. It is highly probable that a certain part also is produced in the system by synthesis. Uric acid excretion is, therefore,

dependent upon a number of factors and its amount may depend upon variable conditions. As matters of practical experience we know that the amount of uric acid in the urine is increased in leukemia, during the resolution of pneumonia and in certain cases of nephritis. The erroneous impression prevails that there is an increase of urinary uric acid in gout and in a variety of undiagnosticated conditions summarized under the captions of uric acid diathesis, lithemia, and the like. This mistaken idea is founded upon the fact that uric acid calculi are prone to form in such conditions and that deposits of urates or of uric acid crystals are likely to occur in the standing urine. The chemists have taught us over and over that these results are due not to increased excretion of uric acid, but to conditions in the urine unfavorable to the solution of uric acid or its compounds. No fallacy has been so difficult to combat and to banish from the world of practical medicine. The lesson cannot too often be repeated that the apparent amount of uric acid as determined by the sediments or crystals seen in the urine and even the accurate quantitative determination of the uric acid by chemical means are practically valueless as diagnostic indications of gout. It was long ago contended by Garrod that there is in gout an increase of uric acid in the blood and his familiar experiment of suspending a thread in the blood serum of a gouty person to observe the formation of crystals has more or less demonstrative value. Later studies by more accurate chemical methods (Duckworth, Klemperer, Magnus-Levy) confirmed his contention and established the fact that there is an increased amount of uric acid in the blood of gouty persons. So far as the elimination in the urine is concerned, the investigations of His and Magnus-Levy have shown a diminution before acute attacks, an increase during attacks, and practically normal amounts between the paroxysms. The figures, however, are not sufficiently striking to furnish any practical aid in the diagnosis of any stage of the disease. It would carry me too far to discuss the various theories that have been constructed to explain these quantitative relations of uric acid in the blood and urine, and the tendency to uratic precipitations in gout. Very recently some evidence has been adduced to show that there is a retardation in the formation of uric acid by oxidation of the nucleinic purin and instead a synthetic production of uric acid, which, on account of the absence in that case of thymic acid with which uric acid ordinarily circulates, is present in a less soluble and more readily precipitable form. It is clear that purin metabolism and the formation of uric acid are intimately connected with the pathology of gout, but it is a complete fallacy to base any attempted diagnosis of that disease on studies of the urine. An older theory (Kolisch) which assumed a retarded transformation of purin bodies into uric acid, though at first attractive, was founded upon analyses made by a faulty method. As for the so-called "uric acid diathesis," we must recognize that this is wholly suppositious. Knowledge regarding this is in inverse relation to the bulk of the literature bearing on it.

Carbohydrate Metabolism. Disturbance of the metabolism of carbohydrates is the most important process in pathological physiology so far as the chemical means of diagnosis are concerned. It must be recognized that the presence of sugar in the urine is not the invariable result of faulty carbohydrate metabolism; nor does glycosuria invariably indicate such a metabolic disorder, but in the main this assumption is justified when glucose is recognized in the urine. The chemical methods, therefore, here assume an importance in diagnosis that cannot be underestimated, and the same methods are further valuable in distinguishing glucose from other reducing bodies (glycuronic acid, the alkapton bodies, and pentoses) which are found in quite different and far less important diseases. The recognition of the latter is wholly the province of chemical investigation.

Fatty Metabolism. In the normal katabolism of fat, it is probable that acetone, diacetic acid, and oxybutyric acid are to some extent produced. In abnormal destruction of fat as in inanition, infections, fever, and diabetes, but especially in the latter, these bodies are often made in increased and sometimes destructive amounts. There results from this one of the known forms of acid intoxication or acidosis, the only genuine auto-intoxication, in the strict sense, with which we are familiar. Chemical methods have furnished us with a more or less complete understanding of such conditions as well as with the power of diagnosticating their approach or existence and with measures of treatment that sometimes prove most valuable.

Before entering on a more extended reference to the question of acid intoxication, let me recall to your minds some of the chemical modes of defence of the organism against toxic agents as of fundamental importance to the understanding of acidosis in particular. The principal of chemical *detoxication* by the pairing of toxic bodies, whether endogenous or exogenous with defensive substances of various sorts, is one of far-reaching importance. Thus the indol and skatol of intestinal putrefaction after a preliminary oxidation are combined with sulphuric acid and eliminated as less toxic sulphates; to a less extent they combine with glycuronic acid. A familiar example of the same process of pairing is that by which glycocol combines with benzoic acid to form hippuric acid. Similarly sulphur may detoxicate cyanogen compounds by forming sulphocyanides; or bile acids may unite with various alkaloids. Far more frequent is the association of acids with cations. The final elimination of nitrogen as urea represents the normal physiological type of this process, urea being the result of a combination of ammonia derived from proteid destruction with carbonic acid. In experimental investigations the direct administration of acids is followed by the combination of these acids with the

fixed cations of the body and, when these prove insufficient, with ammonium. The intermediary metabolism is normally attended with a certain amount of acid formation of various kinds, and under pathological conditions these acids are increased in amount, the katabolism of proteids and nucleins furnishing sulphuric and phosphoric acids, carbohydrate metabolism supplying lactic acid, and in the fats diacetic and oxybutyric acids. When the salts of the food prove insufficient for neutralization, the acids appropriate the fixed cations of the body first and then ammonium for the purpose of neutralization. At some stage toxic symptoms appear. We need not here enter into a discussion which would necessarily be extended, as to the exact cause of the symptoms, whether due to the acidosis as such, to the particular form of acid, or to the withdrawal of the fixed cations or deviation of ammonium. Clinically the phenomena of acid intoxication are most familiarly recognized in cases of diabetes, but their occurrence in starvation, in wasting diseases, in destructive hepatic affections, in certain gastro-intestinal diseases, notably in children, after anesthesia, in puerperal toxemia and occasionally without discoverable origin must be recalled. To what extent minor grades may play a part in various other conditions remains to be dertermined. The fundamental importance of the condition needs no discussion and the chemical method of diagnosis alone avails for its timely recognition and for the direction of effective treatment. I shall have occasion to refer very briefly to the question somewhat later when considering the chemical methods of investigating hepatic disease.

It is necessary now to leave the consideration of general metabolism without attempting to discuss such important questions as sulphur and phosphorous metabolism, the elimination of calcium and magnesium or various metabolic disorders of more or less independent nature like alkaptonuria, pentosuria, cystinuria, and oxaluria, all of which depend for proper recognition and appreciation on refined chemical methods. To mention them suffices to indicate that chemistry has proved no mere embellishment in modern medicine. Without this aid their identification would have been impossible and their mere recognition almost equally so.

Not unnaturally the clinician turned to the chemist for aid in recognizing the beginnings of various organic diseases and the existence of defective organic functions when the resources of morphology and ordinary physical diagnosis were exhausted. The diagnosis of liver diseases (cirrhosis or degenerations) at a stage of advancement at which recovery is hardly possible, the identification of renal disease in its fully developed grades and recognition of gastro-intestinal disorders of advanced type ordinarily present no great difficulty to the clinician, since the pathologist has made us familiar with the association of certain clinical manifestations with the pathological lesions; but the newer aspirations of medicine demand a recognition of organic derangement before destructive changes have become advanced to irremediable stages, and except in the case of the heart, lungs, and nervous system the methods of physical examination are confessedly insufficient. From the beginning of more exact scientific medicine the study of the blood has held out hope of solution of problems of this sort, a hope fanned to more active flame by the introduction of Ehrlich's fascinating methods of blood examination. But neither this morphological method nor the older as well as recent chemistry of the blood have availed us much. Direct chemical examination of secretions and excreta have aided somewhat, but it must be confessed that more than much remains uncertain.

Chemical Diagnosis of Kidney Disease. Enough perhaps has been said regarding the recognition of albuminuria as a symptom of kidney disease. The fact that albuminuria may occur without renal disease does not detract from the value of this sign when disease of the kidney exists. Meltzer has very well said that the natural history of kidney disease was known for centuries before Bright's investigations, but it was the merit of this observer and of his observations that the positive recognition of disease of the kidney became possible. With his help the symptoms of the disease became more accurately known and even in the absence of tests for albuminuria the informed clinician is now able to recognize nephritis. Without this test, however, the clinician, no matter how skilled, is deprived of a most effective method of diagnosis. That albuminuria occurs without nephritis and perhaps certain types of nephritis without discoverable albuminuria needs no particular discussion here. The fact remains that *constant albuminuria* is an indication of renal disease in the absence of definite disproof.

A word is sufficient to recall the value of the recognition of Bence-Jones albuminuria as an indication of disease of the bone-marrow. The early hope of aid in diagnosis from the determination of other albumoses or peptone has proved deceptive. At the present time such determinations seem valueless.

In connection with other examinations of the urine mention may be made in this place of the diazo reaction introduced by Ehrlich for the diagnosis of typhoid fever. The test is well known and its limitations generally recognized. The negative value is far greater than the positive, since there are very few cases of typhoid fever in which the diazo reaction fails during the stadium of the disease, but on the other hand there are quite a large proportion of cases of scarlet fever, pulmonary tuberculosis, pneumonia, measles, and other infections in which it may occur. The exact proportion of cases of typhoid fever in which the reaction occurs cannot be stated, but seems to be well above 90 per cent. In febrile sequelæ not due to reinfection the diazo test fails, while in true relapses it reappears. The presence of a positive

reaction in cases of meningitis or articular rheumatism, in which it is nearly always absent, or in pneumonia, pulmonary tuberculosis, and other conditions in which it is more frequent, has a certain prognostic value, being rather significant of an unfavorable outlook. On the whole the diazo reaction must be regarded as a distinctly valuable addition to our diagnostic methods, though its early promise has not been fulfilled.

Chemical Indications of Renal Sufficiency. Numerous tests have been proposed, but thus far none seems to offer definite hope of permanent usefulness in this direction. Various substances have been administered with the idea that their prompt or tardy elimination in the urine might give some indication of the functional capacity of the kidney. Thus salicylates and iodide of potassium have been used by the mouth or by hypodermic injection, and tests of the urine made after fixed intervals of time; similarly methylene blue has been given and the time of first and latest discoloration of the urine noted; but the results of these methods have proved so variable and inexact that little confidence can be placed in them. A more recent procedure has been suggested by Claude and Mantè and other French clinicians. This is based upon the assumption that a diseased kidney eliminates ingested chloride of sodium less readily than the normal organ. A final judgment regarding this method may not as yet be justifiable, but its value is certainly improved. The phloridzin method is, perhaps, more trustworthy. If a hypodermic injection of 1 c.c. of 1 to 200 phloridzin solution is administered to a normal person, sugar will appear in the urine in from one-half to one hour and will continue to appear during from two to four hours. A more tardy appearance, or the failure to appear, would signify the existence of renal disease. Further investigations of this method are desirable. In the case of any of the methods based upon renal excretion a certain skepticism is necessary, since the promptness of elimination depends upon other factors than elimination alone.

Chemical Indications of Hepatic Disease. The chemical method is of little value in the recognition of jaundice when direct inspection of the patient's skin and mucous membrane fails to reveal that condition. Still there are instances in dark-skinned persons, and occasional cases in persons not dark skinned, of very mild icterus (associated with cirrhosis of the liver, for example) in which the demonstration of bile in the urine or in the blood serum may be possible when inspection gives uncertain indications. In cases of beginning cirrhosis of the liver, particularly, I have found the frequent or continuous presence of traces of bile in the urine unattended with visible jaundice.

Next in importance to the recognition of bile in the urine and in some cases of greater value is the discovery of considerable quantities of urobilin. This chromogen is normally eliminated in small quantities, but is present in considerable amount in diseases of the liver (atrophic cirrhosis) as well as in conditions of blood destruction (as in infections, intoxications, anemias, or after extravasations of blood into the tissues), in certain intestinal conditions and in carcinomatous cachexia. While therefore lacking the directness of a certain indication of hepatic disease, its presence in abundance may, under some circumstances, be highly significant. The methods of recognition are so simple that a more general use of the test is desirable.

Various methods have been proposed for the determination of insufficiency of hepatic function, based upon a recognition of the normal physiological processes. One of the first of these capacities of the liver to be recognized was its power to store up or destroy sugars.

Alimentary Glycosuria. Ingested carbohydrates are, in part, converted into glycogen and in part utilized in anabolic processes or burned. The liver seems to be intimately concerned in their final disposal and when the organ is diseased the assimilation of carbohydrates is presumably lessened. It would seem possible, therefore, to determine the functional activity of the liver by administering known quantities of sugar and observing whether or not excretion takes place in the urine. In normal individuals the limit of assimilation for glucose given to the fasting subject is about 100 grams. When quantities above this figure are administered glycosuria occurs. In some cases of hepatic disease alimentary glycosuria has occurred with decidedly less quantities, but on the other hand advanced liver disease is by no means incompatible with quite a normal power of assimilation of sugar. In addition, it is well known that alcoholism, various neuroses, and exophthalmic goitre may occasion reduced assimilation of sugars even more definitely than any form of hepatic disease. Recently it has been suggested that the administration of levulose followed by the occurrence of alimentary levulosuria (Sachs, Strauss, Lépine) is a more reliable test, but this too has failed of general confirmation.

Urea Formation. The fact that ammonium is converted into urea in the liver has suggested the administration of ammonium salts and the estimation of the excretion of urea as a possible method of estimating the function capacity of the liver. The results of different observers have varied, some finding in hepatic diseases a reduction in the power of conversion of ammonium into urea and consequently the appearance in the urine of the unaltered ammonium salts that were administered; others finding increased output of urea or results that varied without apparent reference to the hepatic disease.

Partition of Nitrogen. Recently the partition of nitrogen eliminated in the urine has been very carefully studied as a possible indication of hepatic disease. It cannot be doubted that in cases of severe disease of the liver the urea nitrogen falls and the ammonium nitrogen and undetermined

nitrogen increase, but there are factors in the probable causation of these changes that are quite independent of a putative disorder of hepatic function and to some extent independent of actual disease of the liver substance. Thus, in acid intoxications independent of hepatic derangement, a similar alteration of nitrogen proportions will be met with. Again, it has been shown by Folin and others that when the total output of nitrogen is greatly reduced by limitation of proteid food or starvation, enormous relative as well as actual reduction in urea nitrogen occurs, with corresponding increase in ammonium nitrogen, kreatinin nitrogen, uric acid nitrogen, and undetermined nitrogen. E. and O. Freund found the urea nitrogen in the professional faster Succi, when in extreme inanition, as low as 54 per cent. to 56 per cent. of the total nitrogen. The nature of the nitrogenous bodies that make up the relatively increased nitrogenous residue is uncertain, but very probably increased quantities of amido acids play an important part. The decreased proportions of urea nitrogen and increased proportions of ammonium nitrogen and undetermined nitrogen found in cases of toxemia of pregnancy by Stone, Edgar, Williams, Ewing, Wolf, and others, cannot therefore be ascribed to functional disturbance of the liver when it is possible that the repeated vomiting in such cases, with possible acidosis, the effects of inanition itself with its reduced output of total nitrogen, and, perhaps, also a disturbance in the normal synthesis of simple nitrogenous cleavage products in the wall of the intestine, might each or all together contribute to the result with or without hepatic disease. Ewing and Wolf contend very strongly for a primary disturbance of metabolism as the cause of the altered nitrogen excretion, but seem to me to undervalue the possible effect of vomiting and inanition independent of either liver disease or any supposititious toxemic state or disordered proteid metabolism. From a practical standpoint it seems to me unwise to assume from altered relations of nitrogen excretion the existence of hepatic disease, unless some other evidence as, for example, an excretion of lactic acid, leucin and tyrosin or other products of intense hepatic disintegration is also shown. These last-named bodies, however, are met with only in cases of extreme hepatic disease and, therefore, have only a restricted value in practical diagnosis.

Detoxicating Function of the Liver. It has been shown that the liver exercises a certain detoxicating function toward various mineral and alkaloidal poisons, such as arsenic, atropine, and strychnine, and its part in the pairing of toxic intestinal products with glycuronic acid may be also recalled. Some rather crude experiments have been made to determine if a reduction of this detoxicating function could be recognized in an increased toxicity of the urine in hepatic disease (Bouchard). Though no practical method has been suggested, further investigations in this direction may prove helpful.

Chemical Determination of Pancreatic Disease. The relation of pancreatic secretion to fat absorption has long been recognized and the occurrence of fatty diarrhea as an indication of pancreatic disease is sufficiently significant to merit recognition. It must not, however, be forgotten that other factors enter into the absorption of fat from the intestinal tract and that considerable grades of steatorrhea may occur independent of any disease of the pancreas or disorder of its secretion. Thus, in jaundice, well-marked fatty diarrhea has frequently been observed, and in intestinal diseases, such as amyloid degeneration, tuberculosis, and simple diarrhea, the same may occur. After the unreliability of the mere presence of excess of fat was recognized, certain investigators suggested that a more important fact is the discovery of excess of neutral fat, showing that the fat-splitting function of the pancreatic secretion is wanting. Müller, von Noorden, Weintraud and Katz, among others, obtained results which indicated the importance of this determination, but on the other hand equally careful studies in cases of pancreatic disease have shown that the splitting of fat was not specially affected. In the absence of jaundice and diarrheal diseases, however, excess of fat in the stools must be looked upon as an important indication of pancreatic disease.

Excess of nitrogen in the feces and the recognition of undigested muscle fibers, like fatty diarrhea, may result from a lack of pancreatic secretion and consequent failure of digestion of proteids. This symptom, however, is of distinctly less value than steatorrhea.

Fat-splitting ferment (lipase) has been sought in the urine as an indication of pancreatic disease. Opie has shown the presence of this ferment in a case of pancreatic disease with fat necrosis, at the same time demonstrating its absence in a non-pancreatic case used as a control. There are, however, several possible fallacies. It must be remembered that lipase occurs in practically all tissues in which fat is found, perhaps exercising a function in these situations as a synthetic ferment operating by reverse action, and it has been demonstrated in the urine by Zeri in a case of hemorrhagic nephritis in which pancreatic disease was not present. There are certain practical difficulties connected with the preparation and preservation of the ethyl butyrate used in the test, and it must be furthermore recognized that ferment action of this sort may be due to varied lipases or to a variety of substances other than fat-splitting ferment.

Cammidge has devised certain tests of the urine to demonstrate the presence of glycerroses (derived from glycerin resulting from the splitting of fat) and has even claimed the ability to distinguish between different forms of pancreatic disease according to the reactions obtained. It would be unprofitable to discuss these tests at length, as they have not been confirmed by other investigators.

Sahli's Method. Glutoid capsules, gelatin capsules hardened in formalin, are supposed to be digested only by pancreatic juice. When such capsules containing iodoform are administered with an Ewald test meal, the saliva or urine will give reactions for iodine at variable periods according to the motility of the stomach and the digestive activity of the pancreatic juice. The precise value of this method has not yet been determined.

The nucleus test suggested by Schmidt is based upon the supposed digestion of cell nuclei by the pancreatic juice, other digestive ferments having no action upon them. In experiments in which the pancreas of dogs was extirpated, the nuclei of meat fibers came through the intestinal tract undigested. In clinical cases Schmidt and his pupils found that the digestion of the nuclei was always accomplished in diseases other than pancreatic disease and usually absent in pancreatic disease. J. Dutton Steele has investigated the subject quite extensively and believes that the nucleus test is probably a rough indication of the presence or absence of pancreatic secretion, but that the relation between the nuclei of muscle and pancreatic digestion may not be specific and that the persistence of nuclei may be the result of a general lowering of digestive power quite as much as the sign of insufficiency of pancreatic secretion.

Ethereal Sulphates and Pancreatic Disease. The ethereal sulphates of the urine are known to be formed by a combination of sulphuric acid with products of intestinal putrefaction of proteids. Since the bacteria of the intestinal tract are more able to cause decomposition of the relatively simple products of digestion than of native proteids, the proportionate amount of such putrefactive bodies (indicated by the amount of ethereal sulphates of the urine) becomes a measure of intestinal digestion of proteids or, in other words, of the presence and efficiency of pancreatic secretion. It has been shown in a number of striking cases that a low proportion of ethereal sulphates in the urine was dependent upon destructive pancreatic disease, and though the value of the test has not been confirmed in some other cases, and though a low proportion of ethereal sulphates may be due to other causes, the occasional value of this test is undoubted.

Glycosuria takes first rank as a symptom of certain pancreatic diseases, but cannot be regarded as positively indicative of such disease, since there is a variety of causes that may produce temporary or even more durable excretion of glucose in the urine. When, however, this symptom is combined with steatorrhea and marked emaciation, the probability of pancreatic disease is very decided, particularly if jaundice is absent.

Chemical Methods in Gastric Diagnosis. The rôle of chemical processes in organic function was first recognized in the case of the stomach and is easily studied on account of the ready procurability of the gastric contents. Not unnaturally, therefore, clinicians have energetically studied the gastric secretions for diagnostic indications. After the introduction of the aniline-color methods of recognizing free hydrochloric acid, and the discovery of the absence of free hydrochloric acid in cancer of the stomach, and the reduction or increase of acid in various other diseases a somewhat undue amount of importance was attached to the chemical methods, which were made the basis not only of diagnosis but also of classification of gastric diseases. With increase of knowledge it has become evident that while a definite and sometimes considerable value attaches to the determination of the absence or presence and the amount of free hydrochloric acid, such estimations can never rank as pathognomonic indications. So far as cancer is concerned, it must be admitted that while the constant absence of free hydrochloric acid is a sign of great value, cases are met with in which free hydrochloric acid is present either occasionally or constantly, and sometimes in excessive amount. Besides, there are other diseases of the stomach (achylia, atrophy of the mucosa) in which constant absence of free hydrochloric acid may occur without carcinoma. Determinations of the amount of hydrochloric acid at different times when the conditions are as nearly alike as possible are of value in estimating the progress of cases of gastric disease; but the ingenuity expended in devising accurate methods for determining the exact quantity of total or free hydrochloric acid in given samples of gastric contents may be regarded as practically wasted effort.

Somewhat after the hydrochloric acid era the presence of a considerable quantity of lactic acid was vaunted as a certain indication of carcinoma of the stomach. It is hardly necessary to discuss in detail the value of this sign. Fuller knowledge has established the fact that lactic acid is formed in the stomach contents when there is stagnation of food and absence of free hydrochloric acid. The determination of lactic acid, a variable end result, is, therefore, somewhat less valuable than the recognition of the factors that give rise to it, both of which are readily demonstrable. As a confirmation test, however, the recognition of lactic acid is of some value, though it is by no means positively indicative of carcinoma of the stomach.

Determinations of pepsin and the curdling ferment have not proved as helpful in diagnosis as has been hoped, and may be regarded as of but occasional and minor importance.

Recently, Sahli has added a method that promises to be of decided value which is carried out as follows: A small rubber bag containing methylene blue is securely tied with catgut so that the contents cannot escape unless the catgut is digested. As solution of connective tissue like that of catgut cannot occur through the action of the pancreatic secretion without the preliminary action of the gastric juice, the bag with its contents will pass through the intestinal tract unopened if gastric secretion is absent. If the catgut is digested the escape of

the methylene blue will be promptly recognized by the blue discoloration of the urine.

Various other chemical tests have been suggested for determining the motility of the stomach and the absorptive power of its mucosa. These are more or less valuable in certain cases, though rarely contributing data of fundamental importance in diagnosis.

Far more valuable than the chemical diagnosis of gastric disease are the physical methods of determining motility, size, and position of the organ with the aid of the stomach tube, inflation apparatus, and skiagraphy. In conjunction, however, with the data so obtained, chemical methods are undoubtedly of some value.

Chemical Methods in the Diagnosis of Intestinal Diseases. Reference has several times been made to the fact that ethereal sulphates of the urine are combinations of oxidized products of intestinal putrefaction with sulphuric acid. Among these intestinal products, indol, skatol, and phenol are most important. The amount produced will depend upon the amount of ingestion of proteid food-stuffs, as it is from proteid decomposition that these substances are derived; furthermore, the degree of decomposition will depend upon the efficiency of pancreatic digestion, as has already been pointed out, and upon local intestinal conditions favorable to the action of microörganisms of putrefaction. Generally speaking, it may be assumed that a persistent high proportion of ethereal sulphates indicates intestinal decomposition, though there are other factors which may occasionally be operative. The attempt has been made to establish, as an index of intestinal putrefaction, the amount of indican (one of the ethereal sulphates) excreted in the urine. Careful investigations have shown that the amount of indican may not be proportional with the total aromatic sulphate excretion, so that in some cases a high proportion of indican may occur with a relatively low proportion of total aromatic sulphates or the reverse. Accurate work, therefore, demands the estimation of the ethereal sulphates as a whole, rather than the indoxyl sulphates alone or any of the others alone.

Enterogenous albumosuria was at one time thought sufficiently distinctive to prove of diagnostic value. In cases of ulcer of the stomach or intestine the administration of albumose in quantities of from 40 to 60 drams is followed by excretion of albumose in the urine. The difficulty of distinguishing various forms of albumose, especially in the presence of albumin, and the variety of conditions under which albumoses occur in the urine, have robbed this test of much of its expected value.

Occult Blood. A recent method that seems to possess distinct value is that by which quantities of blood, too small to cause a visible alteration in the color of the feces, may be recognized by chemical means. The continuous loss of blood in even this slight amount may occasion serious anemia of seemingly uncertain etiology. Such cases may be cleared up by the repeated demonstration of occult blood in the stools. Again a diagnosis of gastric or intestinal ulceration, or carcinoma of the gastro-intestinal tract may be made possible in the same way. The limitations of the test and the conditions under which it should be performed have not, perhaps, been as thoroughly worked out as is desirable. The influence of certain kinds of diet, for example, needs further study, and the frequency with which enough blood escapes to occasion a positive test in such conditions as cirrhosis of the liver, chronic cardiac disease, or other disorders producing intestinal congestion remains to be determined. The possible value of the test, as foreshadowing hemorrhage in typhoid fever, may be alluded to, though final deductions cannot be made.

THE VALUE OF BIOLOGICAL METHODS IN DIAGNOSIS.

Whatever difference of opinion may be regarded as justified in the estimation of the value of chemical methods in diagnosis, surely no controversy can arise regarding the enormous strides that have been made in the more accurate knowledge of infectious diseases and in their more certain diagnosis since the introduction of scientific methods of biological investigation. The powers of observation and acumen of older clinicians like Rush, Louis, and Bretonneau made it possible for clinicians to distinguish between certain forms of infectious disease which have superficial resemblances, but the accurate knowledge of infectious processes necessarily dates from the introduction of biological methods by Pasteur and Koch. The possibility of isolating specific organisms from the bodies of the sick and determining their biological properties presents a means of diagnosis of assured accuracy for the diseases in which the specific organisms have been determined. A wider field of application of biological principles was thrown open by the serum studies of Bordet and Ehrlich and their various followers. With the aid of the cultural methods of Pasteur and Koch and the serum reactions of the latter investigators, a degree of certainty has been attained in diagnosis that must have remained impossible to the older method of clinical investigation, and it may be profitable to review very briefly some of the important relations in which the biological methods have proved practically valuable.

Diagnosis Based upon the Morphological Characters of Discovered Microörganism. There is a certain number of diseases in which the constant presence of a definite microörganism and its peculiar relations to the lesions of the disease establish its probable pathogenicity, though it has been found impossible to isolate the organism in pure culture or even if so isolated to reproduce the disease in lower animals. In such diseases a diagnosis is often established by the discovery of the organism in question. In other cases, though it

has been possible to obtain the organism in pure culture and to reproduce the disease in animals, such results are too difficult for ordinary clinical purposes. Thus, in tuberculosis of the lungs, malaria, amebic dysentery, relapsing fever, Plaut's or Vincent's angina, lepra, trypanosomiasis, and various other parasitic diseases, a prompt and certain diagnosis may be attained in this way. In some others, as pneumonia, gonorrhea, diphtheria, cholera, and influenza, a presumptive diagnosis may be made to be confirmed by the isolation, in pure culture, of the specific organism. Recently there has been added to the list of organisms, which may thus aid in diagnosis, the Spirocheta pallida of syphilis. The exact place of this organism has not yet been positively established, but its constant presence in syphilitic lesions is highly suggestive.

Diagnosis Based on Isolation in Pure Culture of the Specific Organism. It is an every-day experience of practical physicians to call in requisition public clinical laboratories for the diagnosis of cases of diphtheria, and it is well known that without this aid the positive recognition of many cases of the disease would be impossible, while other conditions superficially resembling this disease would, as in the past, be still mistakenly regarded as true diphtheria. In connection with this disease, it is well to recall the fact that the mere presence of a specific microörganism on the surface of the mucous membranes, or sometimes even within the tissues, does not, of necessity, indicate the existence of the specific disease with which that microörganism is related. Thus, diphtheria bacilli may be present in virulent form in the normal pharynx or nasopharynx and may continue to multiply in that situation for considerable periods of time. This fact has sometimes occasioned misunderstanding between practical physicians and public health authorities, but the practitioner should recognize that so far as the community is concerned an individual, though healthy, carrying in his throat virulent diphtheria bacilli, is nearly as dangerous to others as one actually suffering with diphtheria.

Another disease in which the isolation of the specific organism has become of primary importance in diagnosis, especially in obscure cases, is typhoid fever, to which, however, more particular reference will be made in another place.

To the above may be added pneumococcus infections, streptococcus infections, cerebrospinal fever, cholera, influenza, the plague, tetanus, anthrax and glanders, actinomycosis, and a number of others. Not only does the bacteriological method avail in the ordinary diagnosis of these infections, but it has established the fact that some of them may occur in the usual local forms or as a general septicemia. Thus, in the case of pneumonia there may be the ordinary pulmonary lesions with their consequences or, in other cases, a general pneumococcemia; and in the case of the typhoid bacillus exceptional cases may be met with in which the organism has occasioned local or general lesions apart from the usual situation in the intestinal tract.

Diagnosis Based on Isolation of Organisms and Animal Inoculation. In some cases, though the organism is readily discovered and isolated with more or less facility, the final determination of its nature cannot be positively determined until inoculation in animals has been made. Thus, in certain instances, cultures suggesting diphtheria bacilli or those of glanders and plague require the confirmative test of animal inoculation for their positive identification. With the introduction of serum methods the necessity of animal inoculations has been somewhat lessened and the original postulates of Koch may in some cases be set aside, even as to the pathogenicity of a certain organism when serum reactions of a distinctive character are obtained.

Diagnosis Based on Inoculation with Products of Disease. In some cases the isolation of the specific organism, though possible, is so tedious or difficult that a diagnosis is more readily obtained by the direct inoculation of portions of the diseased tissue or pathological exudates. Thus, in the case of tuberculosis, clinicians constantly make use of inoculations of animals with emulsions of the diseased tissues, transudates from the serous cavities, or excretions. This method not only serves to demonstrate the specific nature of the process, but is useful in distinguishing certain organisms, such as the smegma bacillus or various hay bacilli and other acid-proof organisms, from the tubercle bacillus to which they bear a close resemblance.

Recent investigations seemed to indicate the possible usefulness of direct inoculation in the diagnosis of doubtful cases of syphilis, since it has been shown that though most experimental animals are refractive to this disease it may be transmitted to certain monkeys under proper conditions.

SERUM REACTIONS

It would lead too far were I to enter on a discussion of the known or supposed mechanism of various serum reactions, and it is unnecessary to the present discussion to do so. The practical value of some of the more important reactions is of principal interest today. The special advantage of these methods lies in the fact that the serum of the patient alone is necessary, the cultures of the specific organisms to be tested having been obtained from other sources. The serum methods, therefore, possess a considerable advantage over the cultural methods in their ready application.

Agglutination. The agglutination reaction of Pfeiffer has been made available for practical purposes by Gruber, Durham, and Widal. It has been especially applied in the diagnosis of typhoid fever, colon infections, bacillary dysentery, Malta fever, and glanders, and with less success in tuberculosis and some other diseases. Furthermore, the routine

application of this test has led to the discovery of paratyphoid and paracolon infections simulating typhoid fever, and may be hopefully regarded as a possible means of still other differentiations.

The value of the agglutination test or Widal reaction in the diagnosis of typhoid fever cannot be too highly appreciated. Its routine employment by the public laboratories of cities and States has, to a considerable extent, reformed our public records and has in equal measure proved valuable to the practitioner as a guide to proper treatment. In typical cases the physician may not require this assistance, but in many doubtful ones it has served to distinguish between typhoid fever and malaria, or other febrile affections.

It must be remembered that errors are possible in laboratory technique quite as much as in clinical work. The proper performance of the test is of the utmost importance. "Ready methods" of applying it, as in the use of Ficker's *Diagnosticum*, and its general employment by physicians not skilled in laboratory methods, may be regarded as uncertain advances. When carefully performed by an expert the Widal reaction is likely to prove positive at some stage of the disease in from 95 per cent. to 98 per cent. of all cases, and as early as the seventh or eighth day in about 90 per cent. It proves negative in even a larger proportion of non-typhoid cases. There are undoubtedly instances of non-typhoid disease, in persons who have never had typhoid infection, in which a positive Widal test is obtained despite all precautions regarding dilution, etc. Such cases, however, are highly exceptional.

The agglutination reaction is decidedly less valuable in the other diseases in which it has been employed; especially is this true of tuberculosis, in which some certain means of recognizing the infection in its earlier stages is so desirable.

Precipitins. The serum of animals or human beings suffering from various infections will cause a precipitate in the clear filtrate from cultures of the organism causing the infection. The "precipitin" causing this phenomenon is more or less definitely specific; at least the precipitation is manifested to a much smaller extent when a culture of another organism is used. The precipitation reaction has, however, been little employed in the diagnosis of infections. Its greatest usefulness has been found in its applicability to certain medicolegal problems; among others, the differentiation of human from other blood. When any albuminous substance is injected into an animal there develops in the blood serum of this animal, after a certain interval, a specific precipitin which will cause a precipitation of the same albumin from dilute solutions. Thus, when human blood is injected the blood serum of the animal will precipitate dilute solutions of human blood alone, with the exception, probably, of that of certain monkeys. The reaction here is far more specific than in the case of bacteria.

Opsonins. A. E. Wright discovered that the serum of normal persons or those infected with various microörganisms contains a substance or substances which act upon the infecting organisms in such a way as to make them readily susceptible to phagocytic inclusion in leukocytes. The presence of these substances—called *opsonins*—increases the activity of phagocytosis and thus aids in the combat against the infection, while their absence retards phagocytosis and, therefore, enhances the infection. The opsonins appear to be complex bodies having a relatively resistant thermostabile portion and a ferment-like thermolabile portion. It would appear that there are normal opsonins present in every serum and more specific kinds developed by specific infections. The certainty of this distinction requires confirmation, especially if we are to admit the claim of some of the enthusiastic workers in this field, that it is possible to distinguish which one of a mixed culture of organisms was the specific one in a given case by testing the opsonic power of the patient's serum against each of the organisms, and observing which one was most actively appropriated by the phagocytes. As a rule no such definitely specific relation has been claimed for the opsonins, and investigators have been content with determining that the serum of a patient suffering from a certain infection exhibits a high or low opsonic power against the organism concerned in the disease, without attempting to show that the opsonic power was greater in the case of this than in the case of other microörganisms. Even this determination, however, is generally admitted to be difficult, and the range of error is excessive. Some fundamental improvements in the technique are needed, but it is not too much to hope that when such are attained the opsonic method will furnish a useful indication of the susceptibility or insusceptibility of individuals to certain infections, and a useful guide to treatment by vaccination methods. Whatever may be said of the method of quantitatively determining opsonic power (opsonic index), the underlying facts regarding the nature and operation of opsonins seem to be established.

Bacteriolysis. Normal sera frequently exhibit the power of destroying bacteria, and the sera of infected animals or of man suffering with certain infections may present this property in a more or less specific manner, being destructive for the specific organisms concerned in far higher dilutions than are other sera. This specific cytolytic action has been demonstrated very strikingly in the case of trypanosomes by Novy. The principle of bacteriolysis has not, however, been specially developed as a diagnostic aid.

Deviation of the Complement. Recently a new method of diagnosis has been introduced which, if confirmed in its asserted accuracy, may open the way for diagnosis of a variety of conditions, infectious and non-infectious, the specific organisms or causes of which may not as yet be certainly known. The principle on which this method

rests was discovered by Neisser and Wechsberg while investigating the action of rabbits' serum on the vibrio of Metchnikoff. They found that the addition of too much amboceptor prevents the bacteriolytic effect of the immune serum and suggested that the explanation of this is that the amboceptor, uniting with the complement, binds, deflects, or deviates it so that the expected bacteriolysis did not take place. This principle has been applied to diagnosis in a variety of ways and can be best illustrated in a schematic manner.

DEVIATION OF THE COMPLEMENT.

A.

(1) Sheep corpuscles + hemolytic rabbit serum (receptor) + (amboceptor and complement) } = hemolysis.

(2) Sheep corpuscles + hemolytic rabbit serum heated (receptor) + (amboceptor) } = no hemolysis.

(3) Sheep corpuscles + hemolytic rabbit serum heated + guinea-pig serum (receptor) + (amboceptor) + (complement) } = hemolysis.

B.

After incubation.

(1) Antigen (bacterium or diseased tissue, etc.) + homologous serum + guinea-pig serum (receptor) + (amboceptor) + (complement) } = Complement bound.

(2) Antigen + heterologous serum + guinea-pig serum (receptor) + (amboceptor) + (complement) } = Complement free.

C.

B (1) + A (2) = no hemolysis, and indicates that the serum tested and the antigen were homologous.

D.

B (2) + A (2) = hemolysis, and indicates that the serum tested and the antigen were heterologous and left the complement of the guinea-pig serum free to act on A (2) as it did when added directly as in A (3).

A. A hemolytic serum is prepared by injecting washed sheep corpuscles into rabbits. (1) After a certain interval the rabbit serum becomes hemolytic for sheep corpuscles. The sheep corpuscles, having specific receptors, will unite with the amboceptor or hemolytic intermediary body of the rabbit serum; the complement of the same serum again uniting with the amboceptor and effecting the complete hemolysis of the sheep corpuscles. (2) If the rabbit serum be heated the complement is readily destroyed, leaving only the amboceptor; a mixture of sheep corpuscles with such heated serum does not result in hemolysis. (3) The addition now of unheated guinea-pig serum would supply the complement and restore the hemolytic quality of the rabbit serum which had been destroyed by heating.

B. (1) If bacterial bodies, such as typhoid bacilli, tubercle bacilli, meningococci, etc., be mixed with serum or transudates, such as spinal fluid, from diseases corresponding to the bacteria, the amboceptor in the serum will unite with the receptor of the bacterial cell and any added (guinea-pig serum) complement. (2) This union will not take place if the bacterium is not the same as that which was operative in the case from which the serum or exudate was obtained. Thus, if typhoid bacilli were treated with serum from tuberculous cases, no union of the receptor (typhoid) with the amboceptor (tuberculosis) would occur.

The two systems represented in A and B may now be applied in a practical way for the diagnosis of certain cases.

C. Suppose that, as in B (1), typhoid bacilli + typhoid serum + guinea-pig serum be mixed and placed for an hour or more in an incubator. A firm combination of the receptor of the bacilli, the amboceptor in the typhoid serum, and the complement in the guinea-pig serum would result. If this mixture be then added to heated hemolytic rabbit serum [as in A (2)] + washed sheep corpuscles, no hemolysis would result because the complement of the guinea-pig serum, which might have been available to complete the hemolytic system as described above in A (3), has been firmly bound to the amboceptor of the typhoid serum in the preliminary step of the test.

D. If the serum used in the preliminary step was not typhoid serum the receptor of the typhoid bacillus used in the test would not have united with the amboceptor present and the guinea-pig complement would have been left uncombined as in B (2). In that case the subsequent addition of heated hemolytic rabbit serum + washed sheep corpuscles would result in hemolysis because the complement of the guinea-pig serum in this case is free to effect a union with the hemolytic amboceptor in the heated rabbit serum.

Thus, if the organism employed is known and the serum combined with it is unknown, the non-occurrence of hemolysis shows that the two were homologous while the occurrence of hemolysis proves that they were heterologous. A

diagnosis of infectious diseases is, therefore, rendered possible, and has been practically demonstrated in the case of infections with typhoid bacilli, meningococci, gonococci, tubercle bacilli, and other organisms. The test, however, has a far wider applicability, as has been shown in studies of syphilis. In this case, though the specific organism is not certainly known and cannot therefore be used, portions of undoubted syphilitic tissue, such as the liver or spleen of a case of congenital syphilis, may be utilized, for these tissues probably contain the infective organism as well as the specific receptors.

The method has been applied for syphilis in the case of general paralysis and various other nervous diseases, and the fluid from the spinal canal has been used to furnish the amboceptor. A mixture composed of hepatic or splenic tissue of syphilitic origin + fluid from the spinal canal of a case of general paralysis + guinea-pig serum is prepared and after suitable incubation is added to heated hemolytic rabbit serum + washed sheep corpuscles. The non-occurrence of hemolysis shows that the spinal fluid contained syphilitic amboceptors, whereas the occurrence of hemolysis proves the spinal fluid free of syphilitic amboceptors and, therefore, presumably of non-syphilitic origin. As the material for this test would sometimes be difficult to obtain if it were necessary to use fresh tissue from syphilitic cases, several investigators have worked with tissues from infected monkeys and have demonstrated the reliability of this material.

The possibility of still wider application of this test of deviation of the complement extending it to non-infectious processes is shown by the fact that it has been applied successfully in the differentiation of various albuminous bodies by using these bodies as the antigen (receptor) and the serum of animals, which had been injected with the same bodies, to supply the amboceptor. The results of these investigations indicate that the differentiation of egg albumen, serum albumin, and other albuminous bodies by this method is as accurate as that by the older method of precipitin formation referred to before. It is not improbable then that the method of deflection of the complement might be applied to diseases, such as carcinoma and sarcoma, in which the infectiousness, though suspected, may not be hereafter confirmed. Work along this line may not unlikely lead to useful results.

Diagnosis Based on Injections of Bacterial Products. Among the most accurate of all means of diagnosis and one which illustrates the very great value of biological methods in practical medicine is that referred to in the heading. Its application has proved most satisfactory in the case of tuberculosis and glanders.

Diagnostic Use of Tuberculin. It is unnecessary to enter into great detail regarding the diagnostic value of tuberculin. This has been proved by veterinary surgeons, who have the advantage of being able to determine the correctness of their conclusions by killing the animals after the test has been made. These experiments show that the result is positive in at least 95 per cent. of the cases. It is not improbable that in man as high a percentage or even a higher may be obtained. The economic value of this test in the warfare against tuberculosis of cattle may not be passed over without mention. The diagnostic use of tuberculin in man has been restricted by the fear that the dissemination of the disease might be caused by the injections. This fear has substantial ground when large quantities of tuberculin are used, but it is unnecessary to employ larger amounts than from 0.5 to 3 mg. Such quantities, in my own experience as well as in that of those who have used it even more freely, are harmless. It must not be forgotten that a possible error in diagnosis may arise from the fact that an injection of tuberculin may occasion a reaction on account of the presence in some part of the body of an inactive or latent focus of tuberculosis which is not at all connected with the active disease from which the patient at the time is suffering. In this way the mistake of regarding something else for tuberculosis might occur.

Diagnostic Use of Mallein. Though not of especial interest in human medicine, since glanders is a rare disease in man, a word regarding the use of mallein is fitting here as another instance of the aid rendered by biological methods. Veterinarians place the greatest confidence in the accuracy of this test, and it has proved of advantage in the control of glanders among animals.

Having considered, in a more or less general way, the kinds of biological data employed in diagnosis, it may be well to refer more particularly to one or two of the special methods and to the value of applying various biological methods in certain important diseases.

Blood Cultures. The improvements in the technique of blood culture that have been made in the last few years enable the trained bacteriologist to isolate from the blood various microörganisms concerned in evident or obscure infections. Among other diseases typhoid fever deserves mention because blood culture has been the method upon which the final distinction between this disease and the variety known as paratyphoid has been established, and also because culture alone makes it possible to recognize some cases of typhoid fever in which the serum reactions and the clinical symptoms may fail. Next in importance is the aid which blood culture has given in the diagnosis of septicemic conditions. In puerperal sepsis, osteomyelitis, general pneumococcic infection, bacteriologists readily determine the nature of the condition and the biological cause. In two instances I have seen a diagnosis of puerperal septicemia changed to typhoid fever as a result of blood culture at a time when this method only could have established a prompt diagnosis.

Examination of Serous Exudates and Cerebro-spinal Fluid. The importance of careful biological studies of the exudates in the serous cavities in the final diagnosis of the nature of certain cases of pleurisy, pericarditis, peritonitis, arthritis, etc., need only be mentioned. Gonococcic arthritis has been frequently distinguished by this means from other forms, and in many cases could be distinguished by ordinary clinical methods. The same is true of pneumococcic arthritis. Direct culture is sometimes insufficient and the more time consuming method of animal inoculation may be required, especially when the possibility of tuberculosis is concerned.

The comparative safety of the operation of lumbar puncture has placed in the hands of the bacteriologists another kind of material for investigation, and has enabled the clinician, through the aid of bacteriological methods, to distinguish with certainty between meningococcic or other forms of meningitis and tuberculous meningitis. Furthermore, if the test of the deviation of the complement is fully established along the lines of its present promise, it may be possible to distinguish between syphilitic or parasyphilitic and other forms of diseases of the central nervous system.

Typhoid Fever. In no disease have the biological methods of study been utilized to better advantage than in the diagnosis of typhoid fever. After the recognition of the specific microörganism of the disease it was first attempted to establish diagnosis upon the basis of examinations of the stools for the typhoid organism, and, though exceptional bacteriological training is necessary for this examination, the introduction of special media, such as those of Elsner, Piowkowski, and His, has made it possible to distinguish between the typhoid organism and the coli group as well as other confusing forms. In the course of time bacteriologists discovered that the typhoid organism is also excreted from the body through the urine and various investigators found it possible to isolate it in a considerable proportion of the cases of typhoid fever. Furthermore, it was established that a typhoid pyelitis or cystitis might exist for a time after the subsidence of the general infection. Finally, examinations of blood or fluid obtained from the spots in the skin and then cultures of the blood taken directly from a vein were found to give satisfactory results. At the present day the greatest interest attaches to cultures of the blood itself, and with improved methods a positive result is obtained in a large proportion of cases even in the early stages of the disease. It is unnecessary to review the methods employed, but it is well to refer to the peculiar advantage of the bile-containing media of Conradi. With the use of these the amount of blood necessary may be considerably reduced, and not rarely cultures are obtained from such quantities of blood as may be had from an incision into the lobe of the ear or the end of the finger. Usually, however, this amount of blood is rather too small. In a number of cases in my service at the University Hospital, Dr. Klaer has obtained positive cultures before the Widal test was positive and before the clinical diagnosis could be established with certainty.

Before the introduction of these improvements in the technique of blood culture, the reaction of Gruber and Durham, and Widal became a routine procedure in medicine. Its advantages have already been referred to. Finally, for the sake of completeness, reference may be made here to the deviation of the complement as a further possibility. The test of the urine for the diazo reaction has also been mentioned in another place.

Tuberculosis. In many cases of pulmonary tuberculosis the diagnosis is made positive by the discovery of the tubercle bacillus. It must be recalled, however, that there are organisms which bear a puzzling resemblance to this and require differentiation in some cases; more often, however, in suspected renal or intestinal tuberculosis than in the case of the pulmonary disease. Morphological methods are generally sufficient, but sometimes must be supplemented with inoculation of animals and culture.

Inoculation of animals, while a tedious process, has the advantage that it does not require the unusual technical facility which cultivation of the tubercle bacillus calls for even with all the improved methods that have been introduced.

In a few instances of tuberculosis in man, culture methods have been used to differentiate between an originally human or bovine infection. To what extent this differentiation is sound and may be made more common remains for the future to determine.

Much has been said regarding the importance of mixed infection in tuberculosis of the lungs. The attempt to determine a mixed infection by the examination of sputa is crude, inexact, and out of date. Blood culture has, in a certain proportion of cases, demonstrated the presence of the organism causing the secondary infection, but it is probable that in many instances a secondary infection might exist in the lungs, though the organisms of that infection had not, as yet, gained access to the blood. The utilization of serum reactions here opens a hopeful field for investigation, and one which has not yet been taken up to any considerable extent.

It is unnecessary to speak again of the value of tuberculin in the diagnosis of this disease except to express the hope that, if the harmlessness of small doses is found as certain as Trudeau and some others believe, a more general introduction of the method may result. Some other means, however, is desirable for the recognition of this disease before the infection of the lung has become extensive enough to occasion distinct physical signs or the discharge of the bacilli in the sputum. Perhaps the test of the deviation of the complement may fill this role.

Rabies. Though infrequent, this disease is important on account of its severity and, as far as our discussion is concerned, on account of the peculiarly close relation of biological methods to its diagnosis and cure. Two methods of diagnosis are of interest to us. In the first the recognition of the disease depends upon the discovery of certain proliferative changes in the endothelial capsule surrounding the nerve cells of various cerebral and spinal ganglia. These changes described by Van Gehuchten and Nelis in man and animals dead of the disease have been confirmed by a number of investigators. They are not, however, sufficiently regular in occurrence to be wholly satisfactory for diagnosis.

POSITIVE CASES OF RABIES.

	Medulla oblongata.	Gasserian ganglion.	Sympathetic ganglion.
Proliferation changes found in	81 or 66.5%	135 or 100%	28 or 82.4%
No proliferation changes found in	44 or 33.5%	.....	6 or 18.6%

NEGATIVE SUSPECTED CASES OF RABIES.

	Medulla oblongata.	Gasserian ganglion.	Sympathetic ganglion.
No proliferation changes found in	29 or 96.6%	18 or 69.2%	3 or 60%
Proliferation changes found in	1 or 3.3%	8 or 31.8%	2 or 40%

Among the cases of rabies and suspected rabies examined in the Laboratory of the State Live Stock Sanitary Board of Pennsylvania, Dr. Reichel obtained the preceding results.

The second method is that which depends upon the recognition of the so-called Negri bodies. Dr. Reichel's figures here prove more certain.

POSITIVE CASES OF RABIES.

	Hippocampus major.	Cerebellum.
Negri bodies found in	91 or 97.9%	93 or 99%
No Negri bodies found in	2 or 2.1%	1 or 1%

NEGATIVE SUSPECTED CASES.

	Hippocampus major.	Cerebellum.
No Negri bodies found in	26 or 100%	26 or 100%
Negri bodies found in	.....	.....

In two cases, in which Negri bodies were not found, experimental inoculation in animals proved that rabies was present, but subsequent investigation showed that both of these animals had been killed very early in the disease. In the other cases in which Negri bodies were absent the result of animal inoculation was also negative.

THE ABDOMINAL COMPLICATIONS AND SEQUELÆ OF TYPHOID FEVER[1]

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Eberth's discovery of the Bacillus typhosus in 1880 threw much light not only upon the pathology of the fever itself, but upon the multiform complications and sequelæ. Much is now understood that was formerly inexplicable. No disease to which the human organism is subject belongs more exclusively, perhaps, to the realm of internal medicine than does typhoid fever. Conversely, there is no acute infectious disease that can claim so many and diverse surgical complications and sequelæ. Holscher (*Münch. med. Wochenschrift*, 1891, No. 4) has shown that more deaths occur as a result of the complications of typhoid fever than from the fever itself. In a study of 2000 fatal cases he found that 24 per cent. died from the fever per se, and 76 per cent. as the result of the various medical and surgical complications and sequelæ. Nevertheless, in spite of this intimate inter-relation of surgical and medical lesions in typhoid fever, it is singular to note that little or no mention is made of many of these accidents in our modern text-books. It is unnecessary to enter into a detailed consideration of the pathology of typhoid fever, in a treatise dealing essentially with the surgical aspect of the disease; suffice it to cite a few facts bearing directly upon the pathogenesis of the various surgical complications and sequelæ. Flexner (*Journal of Pathology and Bacteriology*, 1894, iii, 202) stated that it was possible to isolate from the blood the Bacillus typhosus in 80 per cent. of cases examined in the early stage of the infection, and

[1] Presented in abstract at a meeting of the Academy of Medicine, Elmira, N. Y., April 3, 1907.

we believe, since the introduction of the Conradi method in laboratory technique, that the percentage will be considerably increased. The blood is the all-important medium of diffusion, being in every case infected, and distributing to the various organs of the human body their respective quota of bacilli. In a single individual they have been found in the mesenteric glands, spleen, liver, bile, kidneys, lungs, bone-marrow, and blood of heart. The viability of the Bacillus typhosus is well illustrated by Schiller's work (*Arbeit kaiserlich Gesundheitsamte*, v, 312) in recultivation of the organism two years following impregnation of threads within the body. Its viability is extraordinary, especially in the spleen, bone-marrow, and bile. Von Dungern (*Münch. med. Woch.*, 1897, No. 26), in a case in which the blood serum gave a Widal agglutination, obtained a pure culture from an abscess found in the region of the gall-bladder fourteen and one-half years after the initial infection; Buschke (*Fortschritte d. Med.*, 1894, 573) in a rib after seven years, and Hunner in the bile after eighteen years. The first observers of the pyogenic property of the bacillus were Fraenkel (*Sechste Kongress inn. Med.*, 1887), Rendu (*La France méd.*, 1885, ii), and Tavel (*Correspondenzbl. schweiz. Aerzte*, 1887). Although in 76.7 per cent. of cases of post-typhoidal suppuration, the Bacillus typhosus was found in "pure culture," it is found very frequently associated with other pyogenic organisms, notably the Micrococcus aureus, albus, and citreus, and the Streptococcus pyogenes. Not infrequently in post-typhoidal suppurations, especially in osteomyelitis and otitis media, pyogenic bacteria alone are demonstrable. Finally many cases have been reported in which at autopsy no intestinal lesions were present, but in which pure cultures of typhoid bacilli have been isolated from various other organs, the spleen, brain, liver, gall-bladder, etc.

The term abdominal complications, when applied to typhoid fever, at once suggests to the surgical mind intestinal perforation, and when a surgeon is called in consultation during the active stage of the disease, perforation is the lesion uppermost in his mind. However, other abdominal crises and complications perhaps less common, but equally serious, occur, and it is to these that this contribution is devoted.

By way of preface a word or two may be said with reference to diagnosis in general. The surgeon is more or less handicapped when he is called upon to give an opinion during the course of the disease, especially as the opinion which he is asked to express often involves recourse to an immediate operation which in the nature of things is a matter of great and serious moment. But more than that; he is handicapped in that, not having seen the patient before, he is not able to make a comparative mental picture of the present condition with that which may have existed a week or more prior to his examination. To be more explicit; in the diagnosis of lesions associated with the intestinal tract we are wont to place much reliance upon certain physical signs, chief among which are tenderness, general and localized; rigidity, general and localized, and distention. In the absence of any complication these signs, one and all of them, may be present in the active stage of the fever. There may be more or less distention and tympany, and the distention may be a very conspicuous symptom. We have all seen cases with alarming distention, which the subsequent course of events proved to be the result of hemorrhage and not of peritonitis. In the active stage of the disease there may be much spontaneous pain and a pronounced tenderness on pressure over the region occupied by the ulcerative lesions, usually in the right iliac fossa. And, again, when associated with localized peritoneal irritation there may be more or less rigidity of the muscles on the right side of the abdomen. Thus in typhoid fever, irrespective of any supervening lesion, we may have present three symptoms—pain, tenderness, and rigidity—which suggest some serious intra-abdominal lesion, usually of inflammatory origin. When compared with the normal state the degree of pain, tenderness, and rigidity is not difficult to estimate. But in recognizing surgical complications in typhoid fever it is not always a question of the presence or absence of these signs, but as to whether they are more pronounced at the time of the surgeon's visit than they were in the course of the disease. As the surgeon has not seen the case before, he must rely upon the statement of the attending physician as to the preëxisting conditions. Finally, the patient is often in a more or less apathetic state as a result of the prolonged toxemia, is less sensitive to pain, and often is unable to give an accurate statement direct or comparative of the sequence of events preceding your visit.

Acute Intussusception. As a complication of typhoid fever intussusception, whether acute or chronic, must be extremely rare. In the 1700 cases covered by Keen in his *Surgical Complications and Sequelæ of Typhoid Fever*, no case of this character was recorded. Since that time (1898) I have been able to find mention of 8 cases: 1 reported by Ross; 2 referred to in Ross's communication; 1 each by Ash and Watkins-Pitchford; 1 by Harte and Ashhurst; 2 referred to in Ash's communication; 1 by Vincent, and 1 by Bryant. 4 of these cases developed during the active stage of the fever; 2 (Watkins-Pitchford and Vincent) during the convalescence. No mention of the period is made in the remaining 2. 4 cases were operated upon and 2 recovered; the remaining 5 were recognized only at postmortem. In the case of Ross the patient had had three hemorrhages on the twenty-first and twenty-fifth days. On the twenty-sixth day the patient awoke with violent abdominal pain without any particular point of intensity; there was some rigidity of the right rectus muscle. The patient screamed with pain and was relieved only by mor-

phine. The temperature was 98° F., the pulse 80, and respirations 20. Two hours after the onset there was a leukocytosis of 16,000; there was a slight increase in the abdominal distention. The case was believed to be a perforation; the abdomen was opened and an intussusception, about two and one-half inches long, was found about three feet from the duodenojejunal junction. The invagination, which was from above downward, was easily reduced and the wound closed. With the exception of two subsequent hemorrhages the patient made an uneventful recovery.

In 5 cases a diagnosis of intestinal perforation had been made; 1 was thought to be either perforation or intestinal obstruction; in 1, peritonitis was so far advanced that no question as to differential diagnosis arose. To mistake intussusception for perforation is excusable since intussusception is, comparatively speaking, so rare a complication and operation is resorted to so early, that the complete clinical picture has not developed. The following features as characteristic of intussusception should be borne in mind: It is more common in males and in children; the onset is sudden, and the first and one of the constant and conspicuous symptoms is pain. During the process of invagination the pain is most acute and may be agonizing in severity, as in 2 of the recorded cases in which the patient screamed with pain; when the parts have become fixed the pain subsides. The pain is colicky and paroxysmal in character, at first widely diffuse, later more or less localized to the seat of the lesion. There may be no vomiting in the initial stage, but diarrhea and bloody stools are characteristic. Comparing the early symptoms of intussusception with intestinal perforation, we find severe pain is constant in intussusception, and the tendency to extreme collapse seems to be greater; rigidity, distention, and localized tenderness are not characteristic features of intussusception until later in the disease when peritonitis sets in, although in Ash's case there was board-like rigidity of the abdominal muscles four or five hours after the initial pain. Intussusception seems much less insidious in its onset, and from the time of onset until the patient is in extremis but three or four hours may have elapsed. This was particularly conspicuous in the cases of Bryant and Ross. In many a case of perforation there may be a reasonable doubt as to the occurrence of any serious abdominal crisis six or even twelve hours after the ulcer actually perforated.

Treves (*Intestinal Obstruction*), in an analysis of 100 examples of intussusception particularly with reference to the etiology, groups 12 cases as due to certain acute and chronic ailments which may or may not have had a concern in the etiology, such as typhoid fever, whooping-cough, cholera, hernia, and cancer. No specific reference is given to any developing during typhoid fever. It is impossible, he says, to assign any definite position in the etiology of intussusception to those various maladies. Not infrequently the association has been purely casual. Probably the debility produced by the previous ailment has been an influential factor. The two most important factors in typhoid fever, I should imagine, would be emaciation and diarrhea. In the cases of Ross and Ash no mention is made of diarrhea, but in the case of Watkins-Pitchford there was a violent enteritis. According to Ash, intussusception in typhoid fever may be due to the interference with peristaltic movements of the bowel caused by the indurated patches at the site of the prëexisting ulcers. The irregularity of the peristaltic action, to which intussusception is attributed in cases of diarrhea, dysentery, etc., would not be an active factor during the stage of convalescence when the patient is on very restricted diet. From the history of the recorded cases the indications for immediate operative intervention are very positive; in every case not operated upon the patients died, the majority of peritonitis. There would seem to be even greater urgency in intussusception than in perforation, since, in the former, the condition becomes desperate in so short a time, that, unless resorted to promptly, operation offers no hope of recovery.

Case I.—Ross (*Trans. Amer. Surg. Assoc.*, vol. vi). Boy, aged seventeen years, was admitted to the German Hospital on the eighth day of an attack of typhoid fever. On the twenty-first day he had a blood-stained liquid stool. The tub baths were stopped, but resumed again on the twenty-fifth day at the patient's request. On this day he had two hemorrhages. On the morning of the twenty-sixth day the patient awoke at 1.30 A.M., with violent abdominal pain, without any particular point of intensity. There was some rigidity of the right rectus muscle. The patient screamed with pain for fifteen minutes and was relieved only by morphine. At 2 A.M. temperature 98° F., respirations 20, pulse 80. At 4.40 A.M. another hemorrhage of 820 c.c. Between the time of onset of pain and 3.30 A.M. there was a slight increase in abdominal distention. There was a leukocytosis of 16,000. It was thought that the patient had a perforation and operation was immediately resorted to. Upon opening the abdomen it was evident that no perforation had occurred. The terminal 20 inches of ileum were moderately distended and showed the typhoid ulcers and bleeding points distinctly through the thin bowel wall. From this point to the duodenum the bowel was completely collapsed. About 3 feet from the junction of the duodenum and the jejunum an intussusception about 2½ to 3 inches long was discovered, the invagination being from above downward. It was readily reduced and the bowel slowly distended. The peritoneal cavity was filled with salt solution and the abdominal wound closed without drainage. On the twenty-seventh day the patient had two hemorrhages: one of 120 and one of 250 c.c. Apart from this the convalescence was uneventful.

Case II.—Ash (*British Medical Journal*, May 3, 1902). Male, aged twenty-five years. On the ninth day of a relapse after a very good night, the patient was suddenly seized with acute abdominal pain which passed off in a short time. The pain returned soon, but was less severe and became continuous. It was referred by the patient to the umbilical and epigastric regions, and on palpation most marked in the umbilical region. Tendency to vomit was almost constant. Pulse rose to 125; the expression of the patient was drawn and anxious; perspiration was profuse. There was board-like rigidity of the abdominal wall, but no distention. The case was regarded as one of peritonitis due to perforation. Operation was performed six and one-half hours after the onset of the symptoms. When the patient was relaxed a tumor was found in the right inguinal region, apparently spherical in form and dull on percussion. The intussusception was in the ileocolic region, forming a tumor about 6 inches long. There was considerable difficulty in attempts at reduction. A portion of the ileum above the intussusception was indurated in patches formed by the healing of confluent enteric ulcers.

The patient made an uninterrupted recovery.

Case III.—W. Watkins-Pitchford (*British Medical Journal*, September 6, 1902). The patient, a male, aged twenty-nine years, having recovered from an average attack of enteric fever, had been going about and taking solid food for more than six weeks although his debility was still marked. On May 24 he had been seized with diarrhea, for which he was dosed with a stock mixture and ordered to bed. The following day the diarrhea still continued and he was suddenly seized with great abdominal pain; vomiting was quite frequent. On the second day he was in a condition of collapse: subnormal temperature, cold extremities; pulse, expression and attitude were "peritoneal." There was frequent vomiting and the passage, during paroxysms of pain, of liquid stools mixed with blood. The abdomen was rigid, retracted, and tender. Although the vomiting and diarrhea gradually ceased, the patient died on the sixth day of the disease. The autopsy reports record that there was no peritonitis. There were nine intussusceptions in the small intestines, two of them double. The lower two or three feet of the ileum presented several healed ulcers, evidently enteric in origin. The cause of death was believed to be acute enteritis of a severity sufficient to suggest the agency of an irritant poison. There was not the slightest evidence, however, to support this suggestion. The intussusceptions were probably of "agonic" variety, but their number and extent make the case an exceptional one. Of the factors operative in the production of intussusception, abnormally active peristalsis was the most important. The debility of the patient and the induration of the bowel, however, may have played some part.

Case IV.—Harte and Ashhurst (*Annals of Surgery*, vol. xxxix) report that they have seen a case of intussusception occurring during an attack of ambulatory typhoid fever, but as the peritonitis was well advanced no question of differential diagnosis arose.

Case V.—J. Vincent (*Archiv. de médecine et de pharmacie militaires*, 1895, xxv, 400) cited by Roberts (*Annals of Surgery*, August 1906). At the end of the seventh week during convalescence from typhoid fever the patient was suddenly seized with abdominal pain and vomiting. "Up to that time the typhoid fever had shown nothing unusual, and was of moderate severity and devoid of special symptoms. The diarrhea had disappeared, and the patient had been free from fever for about two weeks. The man showed depression and complained of a little dull and diffused abdominal pain, with occasional colicky attacks. Below the navel and especially above the pubes marked pain on pressure was present. Vincent was uncertain whether intestinal obstruction or perforation existed. Necropsy disclosed an invagination of the jejunum about 30 cm. below the duodenum, which completely obliterated the lumen. The invagination was downward and about 5 to 6 cm. of the bowel were engaged. At a point below, a second invagination was found, but here the obliteration of the calibre was not complete.

The typhoid lesions were cured and showed no trace of cicatricial contraction or ulceration.

Cases VI and VII.—Cited by Ash (*British Medical Journal*, May 3, 1902). Jennings, during his previous experience of enteric fever in India, has seen two necropsies in which ileocolic intussusception was present. In each case death followed symptoms simulating peritonitis due to perforation of an enteric ulcer.

Case VIII.—Bryant (*Medical Record*, November 18, 1905). The patient, aged twenty-three years, in the first or second week of the disease was suddenly seized with pain in the right iliac region, so severe that he cried out and seemed in great distress. His temperature was 102.3° F.; the pulse rose from 100 to 120, and was very weak; respirations, 24. Fifteen minutes later the pain was less severe; pulse, 130; leukocytes, 7300. The abdomen was extremely sensitive; the tenderness most marked 1 inch above McBurney's point. At 10.30 the temperature was 103.8° F., pulse 140. At the operation an intussusception was found about 8 inches long, invaginated both ways, and a short distance from the ileocecal juncture; a short distance farther on there was a second intussusception about 5 inches in length, also invaginated both ways, and farther on a third about 3 inches long invaginated from the right. The patient died about five hours after the operation. The characteristic features were the suddenness of onset with rapidly oncoming signs of collapse and the multiple type of intussusception.

TABULATED PRESENTATION OF SYMPTOMS IN EIGHT CASES OF INTUSSUSCEPTION.

Cases	1	2	3	4	5	6	7	8
Time of onset	Twenty-sixth day	Ninth day.	6 weeks after recovery.	....	Seventh week	.....	..	First or second week.
Pain	Abdominal.	Abdominal.	Abdominal.	...	Abdominal.	Symptoms simulating peritonitis.	Symptoms simulating peritonitis.	Right iliac region.
Muscular rigidity	Yes.	Yes.	Yes.	...	...	.....	....	Sensitive.
Vomiting	No.	Yes.	Yes.	....	Yes.	.....	....	No.
Highest pulse	80.	125.	.....	....	....	.....	.....	140.
Lowest temperature	98° F.	.. ..	.....	....	....	.....	.....	102.3°.
Highest temperature	98°.	.....	.....	...	.. ..	....	...	103.8°.
Diagnosticated as	Perforation.	Peritonitis, perforation	. .	...	Intestinal obstruction or perforation.			
Leukocytosis	16,000.	.....	.....	...	.....	.....		7300.
Seat of intussusception	3 inches from junction of jejunum & duodenum.	Ileocecal.	Small intestines.	...	Jejunum 30 cm. from duodenum.	Ileocecal.	Ileocecal.	Short distance from ileocecal junction.
Single or multiple	Single.	Single.	Multiple.	....	Multiple.	.....	.....	Multiple.
Operation	Yes.	Yes.	No.	....	No.	.....	.....	Yes.
Result	Recovered.	Recovered.	Death.	...	Death.	Death.	Death.	Death.

VOLVULUS. Volvulus is another of the possible abdominal crises which has been overlooked as a complication of typhoid fever, or if not overlooked has seldom been recorded. All told, the available references to the subject include but 7 cases. As a concrete example of the manner in which this complication may manifest itself, I will cite 1 of the cases.

CASE I.—Eustis (*New Orleans Medical and Surgical Journal*, 1904–05, vol. lxii, 816). During the period of convalescence of an apparently uncomplicated case of typhoid fever, with no abdominal pain, the bowels moving freely once or twice a day, fifteen days after the temperature had gone down to normal, the patient was suddenly seized with violent abdominal pains referred to the umbilicus, followed by vomiting, first of mucus and later of bile-stained fluid. When first seen the patient was in extreme collapse, vomiting almost incessantly, and the stools were green, loose, and offensive. There was little tympanites, marked abdominal rigidity, and tenderness. No mass of any sort could be felt; there was a leukocytosis of 15,000; the patient did not react from shock and died about twenty-four hours after the attack of illness. At the autopsy a volvulus was found about the middle of the jejunum, which was extensively congested and almost gangrenous. The ileum presented ulcers of Peyer's patches several of which had extended almost to the serosa; at the site of the volvulus the intestines were adherent.

Of the various factors recognized as concerned with the production of volvulus, diarrhea and localized peritonitis are the only ones which might be said to have any bearing in typhoid fever. Eustis says, "We can readily appreciate the ease with which a volvulus might develop in cases recovering from typhoid fever, on account of the localized peritonitis so often seen in this disease." The fact that the volvulus involved the small intestine in the 3 cases in which the seat is mentioned would lead one to believe that the more or less localized peritonitis in the neighborhood of the typhoid lesions ought to be recognized as an important etiological factor.

The significant feature in all the cases was the failure in each instance to recognize the true nature of the lesion. Holscher, of Wiesbaden (quoted by Roberts), in a study of complications in 2000 fatal cases of typhoid fever, found an ileus or twisting of the intestine in only 3. In both of Eustis' cases the condition was believed to be a perforation, and the volvulus was discovered only at autopsy. Roberts operated because the symptoms indicated "some intra-abdominal lesion." The records at our disposal are too limited to make any general observations or to draw any conclusions; suffice it to say that in 3 instances the complication developed during the active stage of the disease and once during convalescence. There are no details of the remaining 3. In 2 *extreme collapse was a conspicuous feature from the patients who did not recover:* 1 dying on the first and 1 on the second day. In 1 there was a leukocytosis of 15,000; in 2 diarrheal movements, persistent

vomiting, and signs of general peritonitis, tympanites, rigidity, and tenderness. There is some doubt as to whether there was a volvulus in the case of Roberts. None was recognized during the operation, but Roberts concluded, from the appearance of the bowel at the operation and the immediate relief subsequent thereto, that the symptoms were due to a sudden twist of the ileum, which was disentangled when the coils of intestine were being turned over and over in an endeavor to bring the cecal end of the small intestine up from the pelvis. Duliscöuet's experience was interesting because four days prior to the formation of the volvulus the patient had been operated upon for intestinal perforation.

As in perforation, intussusception, ruptured mesenteric gland, so with volvulus, the patient's only hope of recovery is in recourse to operation. In volvulus of the colon high colonic injections are sometimes successful, but as the seat of predilection in typhoid fever is the ileum or ileocecal region the chance of reducing the volvulus by any means other than operation would of necessity be remote. The collapse may be so extreme as to make the question of operation practically prohibitive. Under any circumstances it would be proper to defer operation, at least for a few hours, until there are some signs of reaction.

Case II.—Eustis *(loc. cit)*. Colored female, aged fifteen years. The patient was first seen July 22, 1903. She was then delirious, temperature 103° F., pulse 134, and respirations 36. An examination of the lungs and heart was negative; the urine contained some bile. Widal reaction was negative and there were no plasmodia malariæ and no leukocytosis. The patient was in a condition of extreme prostration, with distention and extreme tenderness over the abdomen. The patient died five days after her admission to the hospital, her condition having changed but little except in so far that the constipation, which had existed for several days after admission, was followed by severe diarrhea. Autopsy discovered the intestinal lesions of typhoid fever. There were no perforations, but the intestines were matted together with recent adhesions. There was a twist of the ileum about 4 feet above the ileocecal valve.

Case III.—Duliscöuet *(Anjou méd., Angers*, 1899, vi, 193, cited by Roberts) reports a case of laporotomy for intestinal perforation; four days later a second abdominal section was required because of the twists of the abdominal loop.

Case IV.—John B. Roberts (*Annals of Surgery*, vol. xliv, August, 1906). A girl, aged nineteen years, was in the Polyclinic Hospital, under the care of Dr. David Riesman for typhoid fever; she had been admitted on February 9 and showed the usual symptoms of that disease. At 9 P.M. on the 22d she began to complain of abdominal pain of a severe character, which persisted throughout the night. On the next morning the patient was listless, with contracted pupils and parted lips, and had a temperature, at 2 A.M., of 103.4°; at 8 A.M. of 102.4°. The pulse had not varied much from what it was before the pain occurred, but her respiration was increased. The breathing was mostly abdominal in type. There was slight fulness in the lower right quadrant of the abdomen and extreme tenderness in that region, with marked rigidity and some dulness and impaired resonance. The pain was most marked at McBurney's point. At intervals the resistance lessened. There was no tenderness in the right flank posteriorly. The pulse was of good volume, but dicrotic. The liver dulness was preserved and extended to the costal margins. The heart sounds had good tone and were normal. The tongue was dry and could not be readily protruded. At 11 o'clock in the morning of the 23d, tenderness and rigidity were more marked than at 10 o'clock. When Roberts saw her on the 23d at 11.30 A.M. the whole abdomen was rigid, but the rigidity was much more marked in the right iliac region. There had been no sudden drop in temperature, though in the preceding thirty-six hours the temperature had come down about 3°, and there had been a slight increase in pulse and respiration. At the time of the examination, however, the condition of pulse, respiration, and temperature was about that which had existed prior to this gradual fall of temperature. The patient was crying out at intervals from pain, and gave evidence of great pain when the skin over the right iliac region was even lightly touched. This occurred even if her attention was distracted from her abdomen, by asking her to put out her tongue. The general symptoms of perforation were not present, but the pain, tenderness, and rigidity seemed to indicate some intra-abdominal lesion.

At the operation nothing definite was found to account for the symptoms. In view of the subsequent improvement and recovery, Roberts concluded that the symptoms had been due to a twist of the ileum which was finally disentangled when he turned the coils over and over in the endeavor to bring the cecal end of the small intestine up from the pelvis in which it was imprisoned.

Mesenteric Lymph Nodes. Rupture of inflamed mesenteric glands as a complication of typhoid fever has been pointed out by a number of observers (Scott, McCrae and Mitchell, Harte and Ashhurst, and Rowland). The ileocecal lymph nodes are the most commonly affected (Le Conte), because of their relation to the most common seat of the typhoidal lesions. The processes may be classified under two headings: (1) the acutely swollen and inflamed or non-suppurative, and (2) the suppurative, which may progress to rupture, peritonitis, and death. In a review of the literature we have been able to collect but 8 authentic cases of suppuration, and in 2 of these (Thomson's and Law's), there is some doubt as to whether the infection was typhoidal. Of these 8, 5 were operated upon, with 4 recoveries, All the cases not operated upon died. In 1

case the abscess ruptured into the superior mesenteric artery, causing death; in another into the bowel, the result not being stated, and in 2 cases (Le Conte's and Frazier's) into the free abdominal cavity. In contrast to the infrequency of suppuration and rupture, acute inflammation giving rise to symptoms suggestive of some grave abdominal condition is very common; in many cases where an exploratory laporotomy for suspected intestinal perforation or appendicitis found no perforation and a normal appendix, the symptoms were in all probability due to mesenteric lymphadenitis. In our collection there were but 4 cases of demonstrable swollen, inflamed nodes (Rowland 2, Sheldon, and Frazier). Rostovtzeff and Quarotski have reported 2 exceedingly interesting cases of hematoma of the mesenteric lymph nodes. One died of some intercurrent affection subsequent to operation. Bacteriological studies demonstrated the Bacillus typhosus in pure culture, as a mixed infection, or entirely absent. Males seem to be afflicted more frequently. Adolescence and early adult life is the age of predilection and the complication may arise early or late in the course of the disease.

The following cases occurred in the experience of one of the writers.

Case I.—Frazier (University Hospital). Typhoid fever complicated by mesenteric lymphatic suppuration. M. H., male, aged twenty-one years, was admitted February 21, 1905, complaining of headache, malaise, and epistaxis. His habits have been bad, especially with reference to excessive indulgences in alcohol and tobacco; his occupations have been many, for the last three weeks prior to admission he was employed in "lead works." The family history is negative.

History of Present Illness. Three days ago, February 18, he began to feel ill, complaining of headache, malaise, lassitude, and general weakness. Two days later epistaxis occurred and again today.

Condition on Admission. February 21, 1905. Temperature 104° F.; pulse, 100; respirations, 36 (6 P.M.). Patient had a typical typhoid expression, with a heavy, languid look and a dusky flush of the cheeks; pupils slightly dilated; pulse dicrotic; spleen palpable; no roscola, but slight tenderness in right iliac fossa.

Blood Analysis. Hemoglobin, 90 per cent.; red blood cells, 4,885,000; white blood cells, 7100.

February 22d. Widal positive. Patient stands the Brandt treatment very well. His general condition is good. A good reaction follows the "tubs" and the pulse is of good quality.

23d. Leukocytes, 7800. Slight tympany; as yet no roscola; spleen not so palpable owing to tympany.

24th. Condition good; pulse is not so markedly dicrotic. Albuminous cloud persists in urine.

26th. Roscola appeared on the abdomen, marking the eighth day of the disease. Enemata are not required for the bowel evacuations; sleeps a great deal; tympany persists.

28th. Subsidence in temperature and increase in roscola. Spleen not palpable.

March 2d. Following a "tub" this evening, the temperature fell from 102° F., to 96.4° F. Although his condition was good the cardiac and respiratory action being unaffected at the time of the fall in temperature, sponge baths were substituted for the tubbing.

3d. Patient's condition excellent, and tympany greatly decreased. Highest temperature, 100.8° F.; pulse, 80; complains of hunger. Leukocyte count, 6100.

7th. Spleen still palpable on deep inspiration; no roscola.

9th. Continues to convalesce slowly. Though the temperature is not falling as regularly as it should the patient's general condition is good; he complains only of hunger. Tonight following a "tub bath" his temperature having reached 102.8° F. fell to 97° F., and the temperature of the water was increased to 85° F. No cardiovascular impairment was noticed.

11th. Leukocyte count, 8600. Urinalysis, trace of albumin and a few hyaline casts. Spleen continues to be but slightly palpable.

15th. Temperature reached normal today for the first time since onset of illness. His general condition is good. His pulse, while slightly dicrotic, is of good quality and of normal rate.

18th. Patient this morning stated that in the night he experienced a peculiar sensation in his abdomen, remarking to a neighbor patient at the time "Something busted then, but did not go all the way."

Leukocyte count showed a sudden increase to 18,000. The patient was immediately transferred to the surgical wards for operation for suspected intestinal perforation.

Operation by Dr. Frazier. Through a right rectus incision a careful search was made for perforation, but with negative results. A small deposit of lymph was observed at one place. Further exploration, however, revealed a necrotic, suppurating mesenteric lymph node, deeply situated and about the size of a horse-chestnut. The opening in the capsule at the site of perforation was enlarged, the contents curetted away and a cigarette drain introduced within the capsule and sutured in place to the capsule with catgut. A wick of iodoform gauze was introduced along the drain, and the wound closed with through-and-through silkworm-gut sutures. Following the operation the patient was placed in the Fowler position and treated as a case of peritonitis. The second day after the operation the leukocytes numbered 7040; the temperature speedily fell to normal, and an uninterrupted convalescence ensued.

Remarks. It is to be regretted that no cultures were made from the necrotic contents of the lymph node. The diagnosis of typhoid fever in consideration of the symptomatology and laboratory tests seemed unquestioned. It is interesting to note that the patient himself was able to state precisely when the distended suppurating lymph node ruptured, from the peculiar sensation of something giving way. The value of leukocytosis as a diagnostic aid in the recognition of the initial stage of peritoneal invasion, as in the preperforative stage, is well illustrated in this case, where the leukocytes rose rapidly from 6000 to 18,000.

Case II.—Frazier (University Hospital). Typhoid fever complicated by acute mesenteric lymphadenitis and acute catarrhal and interstitial appendicitis. This patient is described more in detail with the appendiceal complications of typhoid fever (see Case I). Suffice it to say that with the appendix Frazier removed an enlarged mesenteric lymph node which was the seat of more or less hyperplasia and inflammation. The report from the Laboratory of Surgical Pathology stated that the Bacillus typhosus was found in pure culture, in both the appendix and the lymph node. It is not surprising that the typhoid organisms should be found in the mesenteric lymph nodes, considering their location in relation to the atria of infection. Whether the symptoms in this case were due to the inflamed and swollen lymph node or to the appendicitis is a matter of conjecture, but we are inclined to think that at least some of them were provoked by the lymphadenitis.

The diagnosis of a ruptured suppurating lymph node from perforation or some other intra-abdominal crisis must be a matter of more or less conjecture. According to Rowland of first importance is the presence of a tumor in the right lower quadrant. On rectal examination there may be fulness and tenderness in intestinal perforation, but a movable, tender mass in this region ought to suggest something more. In Rowland's second case such a mass was easily palpable and led to the consideration of appendicitis and tuberculous peritonitis. Dulness in the flanks, obliteration of liver flatness, rapid arrest of peristalsis, tympany and abdominal rigidity point only to a general peritonitis. Immediately after the rupture there will be signs of more or less collapse. In the case under our own observation this was not nearly so pronounced as it has been observed in volvulus, intussusception, and perforation or hemorrhage. The general condition of the patient in connection with the course and the time of disease, the sense of something having ruptured, a simultaneous increase in leukocytosis, suggested the rupture of a viscus and beginning peritonitis.

If it is possible to draw any deductions from our limited number of cases, the treatment should consist in immediate operative intervention. 4 of the 5 cases subjected to operation recovered, and all 3 of those who were not operated upon died. The ideal time for operation might be said to be in the preperforative stage, although it is not likely that we will ever be able to draw the line so finely that we can recognize the lesion before rupture has occurred. Incision should be made to the right of the median line, inasmuch as in most instances the ileocecal glands are involved. Once having found the ruptured node its contents should be removed with a curette and a small cigarette drain introduced, after having carefully wiped off the intestines in the immediate vicinity. The prognosis after these operations, according to statistics, is exceptionally good when compared with operations for any of the other of the more serious abdominal complications.

Appendicitis and Typhoid Fever. Although the involvement of the appendix in typhoidal lesions of the intestines with or without perforation was recognized almost a century ago, the literature shows that the subject was not recognized by surgeons as one of much significance until more recent years. In Keen's excellent monograph on *Surgical Complications and Sequelæ of Typhoid Fever* no mention is made at all of appendicitis. Of the twenty-four contributions to the subject which we have found almost all were published since 1900 and the majority during the past two years.

Incidence. Of 9713 cases of typhoid fever at the Pennsylvania Hospital (Scott, *Proc. of the Phila. County Med. Soc.*, vol. xxv), there were 382 cases of perforation, in 17 of which, or 4.4 per cent., the appendix alone was the seat of perforation. 16 per cent. of what were supposed to be perforations were diseases of the appendix and 5 cases were distinctly due to typhoidal ulcers in the appendix. Ashhurst (*loc. cit.*) found references to 82 cases of lesions of the appendix during typhoid fever. Rolleston (*Lancet*, May 29, 1898), in an examination of 60 cases of typhoid fever, found the appendix affected in 14, 2 of which were perforated, and 7 with distinct ulcers; but while appendicitis is by no means uncommonly associated with typhoid fever, the manifestations, both clinical and pathological, will be found to differ so much that, at least for discussion, a classification into four groups is helpful and admissible:

1. A group in which, at the onset of the fever, the cases are erroneously regarded as appendicitis.

2. A group in which an undoubted case of appendicitis, either of the initial or recurrent type, occurs during the course of the fever, merely as a coincidence.

3. A group in which appendicitis is the direct result of the specific inflammation involving the lymphoid tissue, with or without ulceration and perforation.

4. Lastly a group in which appendicitis develops during the convalescence or later on, and there appears to be some direct or indirect causal relation.

The first of these groups does not belong properly to the

subject under discussion except in so far as it reminds us of the possibility of making an erroneous diagnosis and of jeopardizing the patient's condition by unnecessary and ill-advised operation. How frequently such mistakes are made it is difficult to determine, as they do not find their way readily into literature. The cases in which mistakes are most likely to be made are those in which there is an unusually sudden onset, with an unusual amount of abdominal pain, perhaps vomiting and muscular rigidity. Thus, Oliver (*Cincinnati Lancet-Clinic*, 1905, New Series, liv, No. 1) records a case of a child, aged thirteen years, who three days before admission was seized with severe pain and vomiting. On examination there was found to be marked muscular rigidity, pain and tenderness at McBurney's point, and a palpable tumor. At the operation the appendix appeared to be normal and was not removed. The patient died the day of the operation and the autopsy revealed the characteristic lesions of typhoid fever. An interesting feature in this record was the presence of a palpable tumor, which in the region of the appendix and with other suggestive symptoms would prove most misleading. Curschmann (*Die Unterleibtyphus*, Wien, 1898) has called attention to a condition occurring during typhoid fever which corresponds to the findings in Oliver's case and accounts for the palpable tumor. This consists of a circumscribed inflammation of the peritoneum in the right iliac fossa, involving chiefly the cecum and adjacent portion of the ileum. This process, which he calls perityphlitis typhosa, is due to the extension of the infection to the serosa either through minute perforations or from deep ulcerations where the solution of continuity is almost destroyed.

In some cases this process may terminate in resolution, in others in abscess formation. Thus Thirion (*Journal des sciences de méd. de Lille*, 1905, p. 496) narrates an experience with a case in which, on the seventeenth day of the disease, the patient was suddenly seized with symptoms of acute appendicitis. At the operation the appendix was found retrocecal and perfectly normal, but there was a circumscribed abscess walled in by adhesions between the ileum and cecum. The patient survived the operation but a few hours.

McCrae (*Johns Hopkins Hospital Bulletin*, 1902, vol. x) cites 2 cases which, owing to the sudden onset of the disease, were admitted as cases of acute appendicitis. Neither of them were subjected to operation, and both proved to be cases of typhoid fever terminating in recovery.

The responsibilities of the surgeon in these cases is a very grave one and he should, whenever possible, advise with an experienced physician before deciding either to operate or not to operate. Fortunately, as Richardson says, "operations in the initial stages of typhoid fever are as a rule well borne, and it is the initial stages of the unusual and atypical stages that most frequently suggest appendicitis. A brief and uncomplicated appendectomy would probably have little unfavorable influence upon the subsequent course of the disease. In the case of death in the course of the disease, however, there could never be, in the minds of either the surgeon or the patient's friends, the consoling thought that the early operation had nothing to do with the fatal termination."

Group 2. *Coincident Appendicitis.* There is nothing incompatible with the development of these two diseases independent of one another, although Kelly inclines toward the view that in the majority of cases there will be a history of previous attacks; at all events he failed to find any instance of simple acute appendicitis occurring during the course of the disease. In an appendix already crippled by previous attacks, perhaps with strictures, with kinks, with concretions, or with some mechanical interference with drainage, the swelling of the mucosa incident to an attack of appendicitis may act as the determining cause for a recurrent attack. The pathological process may differ in no respect from that occurring in an otherwise healthy individual.

As an example of an acute incidental appendicitis, I may cite a very instructive case in which almost immediate recourse to operation saved the patient's life. The history of the case as recorded by Jopson (*Annals of Surgery*, 1905, vol. xlii, p. 738) was briefly this: A young girl, aged twelve years, was under treatment for enteric fever; she had suffered for two years with attacks of indigestion so called, accompanied by vomiting and some abdominal pain, lasting several weeks. In about the second week of the disease, there having been no severe abdominal symptoms, she was suddenly seized with violent pain on the right side extending from ribs to pelvis, paroxysmal in type, associated with a chill and vomiting; the spontaneous pain subsided, but there was generalized rigidity and tenderness, more marked on the right side. The leukocytes had risen from 3600 to 10,800; there was a fall in temperature; the pulse and respiration were rapid. A diagnosis of intestinal perforation was made and the abdomen opened eight hours after the beginning of the pain; a perforative gangrenous appendicitis was found with free, cloudy fluid in the peritoneal cavity, but no perforation of the ileum. The patient recovered from the effects of the operation and eventually from the enteric fever. The appendix was gangrenous for about two-fifths of its distal portion and contained in its tip a large concretion. There were no typhoidal ulcers. Abundant staphylococci were recovered from cultures. The case was regarded as one of the chronic or relapsing type roused into activity by the hyperemic and favoring conditions of the enteric attack, but not depending for its origin on any specific typhoidal lesion.

With this case in view, we may consider the most important phases of this subject, namely, the diagnosis and treatment. The diagnosis presents three points of difficulty: first,

the differentiation of typhoid fever from appendicitis in the first stages of the disease, secondly, the recognition of appendicitis in an established case of typhoid fever, and, thirdly, the differentiation between appendicitis and typhoid perforation. In the first of these the diagnosis should be the least difficult, although the sudden onset of the disease has led to erroneous diagnoses. Little reliance can be placed upon the Widal test because it is so frequently negative in the first week or ten days and often until much later in the course of the disease. A careful analysis of the blood count is, however, one of the most valuable signs in distinguishing typhoid infection of the ileum from other lesions such as appendicitis or cholecystitis. Typhoid fever is a disease in which a leukopenia is one of the most constant phenomena. Unfortunately in the first few days the leukocytes may rise to even 10,000 before they begin to fall. At this period the leukocytic count will be of positive value as pointing to an appendicitis only in those cases in which there is a relatively higher leukocytosis. Later on, however, in typhoid fever the number of leukocytes may fall as low as 3000, whereas, an appendicitis, be it ever so mild, will invariably be associated with at least a moderate leukocytosis. The information derived from a differential count is of much greater significance. A relative increase in the polymorphonuclear leukocytes is a far more delicate test not only of the presence of appendicitis but of the patient's power of resistance. This is in direct contrast to the findings in typhoid fever, where there is an increase of the mononuclear leukocytes. It is important in all cases to enquire into the previous history of the patient, whether on the one hand there may have been a previous attack of appendicitis or a previous attack of enteric fever. A history of gradual loss in weight and malaise would suggest enteric fever. Of the four cardinal symptoms, pain, tenderness, muscular rigidity, and fever, Richardson says (*Boston Medical and Surgical Journal*, January, 1902): "Let any of these be absent, and doubt as to the existence of an acute appendicitis arises." Of all the possible combinations, pain, rigidity, and tenderness without fever, would arouse less doubt in the minds of the diagnostician. Before a diagnosis of appendicitis should be made the absence of one or the other of the remaining three, pain, tenderness and rigidity, must be accounted for. With pain and tenderness, the absence of rigidity should arouse suspicion. The same would be true of tenderness and rigidity without pain. When typhoid fever is suspected there may be pain, tenderness, and fever, but the surgeon must account for the absence of rigidity before he opens the abdomen. In summing up his very able and clear presentation of the facts in the differential diagnosis, Richardson says: "After all, the main point to be emphasized in the discrimination between typhoid and appendicitis is that, when any of the local signs mentioned are absent, especially tenderness and rigidity, fever strongly suggests typhoid, and the case must be studied with special care lest typhoid be overlooked; so, too, when the constitutional signs outweigh the local.

"Finally, a few facts should be emphasized. Without pain at some time in the course of the disease, there can be no acute surgical lesion of the abdomen; temperature with pain, but without rigidity or tenderness, means typhoid fever, or should excite suspicion if pain and tenderness are present but not marked, for acute appendicitis has usually a moderate temperature; a soft abdomen with a high temperature is a suspicious combination, even if there is pain and tenderness; when typhoid is suspected, the pain and tenderness must be distinctly localized in the appendix and confirmed by rigidity, resistance or tumor, before operation for appendicitis is justifiable.

"When there is doubt as to typhoid, the operation should be postponed if constitutional signs are severe and local ones hard of detection. When the abdominal symptoms—pain, tenderness, rigidity, with or without distention—call loudly for operation, the abdomen must be opened in spite of the possibilities of typhoid; but cases suggesting typhoid as strongly as appendicitis should, until the diagnosis is perfectly clear, be carefully observed."

Group 3. *Typhoid Appendicitis.* In this class are those cases which Kelly describes as "appendicitis of mild or severe type arising from typhoid affection of the lymph glands or ulceration of the appendix." Thus the pathological lesions in the ileum are present to a greater or less degree in the appendix. There may be congestion of the organ, a catarrhal or ulcerative condition of the mucous membrane, a more or less intense infiltration of the submucosa and muscular coats, with cells typical of the typhoid process, and a fibrinous exudate upon the serosa. The process may vary in degree from an inflammation of the interstitial type of appendicitis to ulceration with or without perforation or even complete necrosis. According to the statistics of Scott (already quoted) in 4.4 per cent. of cases of typhoid, perforations occur from ulcers in the appendix. This is one of the most important and most grave aspects of the relationship of typhoid and appendicitis and is a matter of vital importance when considering the question of treatment.

My first experience of this kind was in the case of a medical student under the care of Dr. Alfred Stengel. During the third week of an otherwise uncomplicated case the patient suddenly developed signs of appendicitis. From the nature of the case there was little doubt as to the diagnosis. The question of operation was discussed on several successive days with the hope that it might be deferred until the convalescence or even later. The process showed no signs of spontaneous resolution within a reasonable time and the appendix was removed. There was a leukocytosis of 17,000. For a week following the operation the range of temperature

was higher than it had been the week preceding; otherwise the course of the fever and the patient's general condition were unaffected by the operation, and recovery ensued. The appendix was intensely congested and swollen, there were several ulcerations but no perforations, no concretions, and no stenosis; the lumen was filled with a mixture of foul-smelling pus and liquid feces. Pathological diagnosis: acute, typhoidal appendicitis. Pure cultures of the typhoid bacillus were recovered from the appendix.

The propriety of operating in this case, even in the light of the pathological findings, might well be questioned. Though ulcerative areas may have threatened perforation at any time, I am now inclined to believe that should similar circumstances present themselves today I would be disposed to wait until there were signs of perforation.

To distinguish appendicitis from typhoid perforation should not, in the majority of cases, be a matter of great difficulty. In appendicitis the symptoms are not suggestive of an abdominal crisis; the disease develops more gradually and does not assume an alarming condition in so short a time. In appendicitis the fall of temperature, the suggestion of shock, the signs of localized peritonitis rapidly becoming general are not so apt to occur. Sudden increase in the rate of the pulse is quite characteristic of typhoid perforation, the pain is often of a stabbing character, and there is distinct change in the facial expression, which is characteristic of the shock of perforation (Harte-Ashhurst). Both typhoid perforation and appendicitis produce rigidity and tenderness. It should be remembered, however, that in typhoid-fever patients the sense of pain is often much less acute, so that the patient's statement as to the degree of tenderness may be quite misleading. An analysis of the blood may throw some light upon the subject, but only when observations have been made sufficiently frequent to catch the preperforative rise and the fall that follows perforation. A rising leukocytosis and a relative increase in the polymorphonuclear leukocytes point to appendicitis. Crile has observed a transitory rise in blood pressure in the preperforative stage due to the initial irritation of the sensitive peritoneum. An attempt to distinguish between an acute gangrenous or perforative appendicitis, as in the case of Jopson, and typhoid perforation need not be made, since the indications for operation would be equally positive in both.

Treatment. The responsibility of opening the abdomen of the typhoid-fever patient is one of the gravest the surgeon has to bear. This responsibility increases in proportion to the duration of the disease, at least up to the point at which the fever is nearly run out. For this reason too much time and thought cannot be spent in familiarizing one's self with all the minutiæ pertaining to diagnosis, and the surgeon should never lose an apportunity of examining typhoid patients in order to keep himself thoroughly familiar with the physical state, particularly, of the abdomen throughout the course of the disease. Are operations upon typhoid-fever patients well borne? Certainly not in operations for typhoid perforation, where the mortality is shockingly high, probably nearer 80 than 70 per cent. Even in exploratory operations with no peritoneal lesions the mortality is 38.46 per cent. (Harte and Ashhurst), and in 27 operations for appendicitis in typhoid-fever patients the same observers found a death rate of 37 per cent. This array of figures sounds a warning to surgeons and changes our attitude toward the question of the operative treatment of appendicitis from one of confident radicalism to one of extreme caution and conservatism. To be sure in the first week of the fever the danger is not so great. In Harte and Ashhurst's series the mortality in the first week was nil, in the second 50 per cent., in the third 75 per cent., in the fourth 100 per cent., and in the fifth week 50 per cent. Thus a mistaken diagnosis and operation in the first week entails little or no risk to life; later than this operation should be regarded only as a measure of dire necessity.

Post-typhoid Appendicitis. Appendicitis as a sequel of typhoid fever is a subject which has attracted attention only in comparatively recent years. The more frequent recognition of it during this period is a tribute to more accurate and painstaking methods of observation and of record keeping. To the latter more than to any other factor are we indebted to many important additions and contributions to the sum-total of our knowledge upon many a subject. We have now on hand data to show that the appendix is not infrequently involved in the specific typhoidal inflammatory process. Owing to the conservative policy now prevalent among surgeons the appendix is not removed except in more or less desperate cases. Upon the subsidence of the process there are no doubt certain permanent structural changes, such, for example, as strictures following ulceration, kinking, and fixation from adhesions and such interference with drainage as might result from the infiltration of its muscular coat. Any one of these factors may predispose toward original attacks. With the exception of this purely hypothetical basis we have little upon which to establish the precise relationship of effect and cause. According to Stokes appendicitis has been produced experimentally through the agency of the typhoid bacillus, and in an investigation of 718 cases of appendicitis Hapgenhausen (*Rev. de la Suisse Rom.*, tome 19, p. 105) found only 36 cases with a previous history of typhoid fever ranging from two months to forty years before the attack of appendicitis. These figures are at least suggestive of the predisposing influence of pre-existing typhoid upon the appendix. The discovery of the typhoid bacillus by Stokes in an appendix removed from a patient thirteen years after an attack of typhoid fever, is another example of the long period which may intervene between the orginal disease and the final elimination of

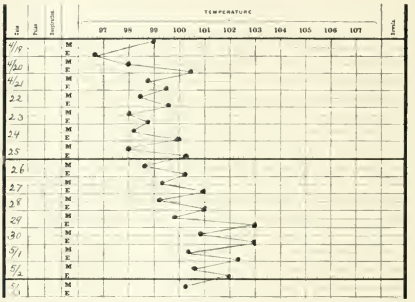
the bacilli. This peculiar feature of the life history of the organism in human individuals has been demonstrated over and over again in diseases of the gall-bladder. Stokes suggests that in his case the gall-bladder may have been the habitat of the organism, but when discharged with the bile into the intestine the normal lymphoid follicles of the appendix proved a more congenial atrium for infection than that afforded by the scar tissue in Peyer's patches of the ileum. The following case may be appropriately considered here as it presented an additional complication close on the heels of enteric fever. The symptoms were those of intestinal obstruction; a large pelvic abscess was found well walled off by a mass of adherent intestines.

Stengel and Frazier (University Hospital). J. W., aged nineteen years, was admitted to the hospital, February 26, 1907, with typhoid fever in the course of which two positive Widal reactions were obtained. He was progressing toward convalescence when he began to show signs of intestinal obstruction. There was complete constipation and he vomited three or four times a day. Upon my first examination his temperature was 98.4° F., pulse 120, and respirations 24. There was extreme pallor of the skin and visible mucous membranes and great emaciation. The thoracic examination was negative. While there was a decided epigastric fulness the remainder of the abdomen was retracted. In the suprapubic region a mass was felt about the size of a fetal head, quite tender to the touch, thought at first, but erroneously, to be an overdistended bladder. There was no dulness in the flanks; the liver extended 2 cm. below the margin of the ribs. The leukocytes were 10,160; a Widal test was negative.

Operation. Exploration under ether discovered a large abscess filling the entire pelvis and completely walled off by a mass of intestines matted together. An attempt to unravel the snarl of adherent intestines seemed unwarranted. The pus was evacuated and drainage introduced. The bacteriologist recovered from the pus the Streptococcus pyogenes. The origin of the abscess was obscure. It may have been due to an appendicitis, to a perityphlitis, or to leakage from an ulcer. The Bacillus typhosus was not recovered from the pus. Whatever the nature of the abscess the case is interesting in that it presented two rather unusual complications; intestinal obstruction and pelvic abscess, either of which called for surgical relief.

Appendicitis as a Forerunner of Typhoid Fever. In direct contrast to the development of appendicitis as a sequel of typhoid fever we may refer to a case in which an attack of appendicitis immediately preceded the onset of typhoid. This is a very unusual sequence of events and therefore worthy of record.

Frazier and Stengel. M. McM., aged eighteen years, was admitted to the University Hospital, May 12, 1904. Two years before Dr. Frazier removed a cervical rib. A year before she had an attack similar in its onset to the present, but lasting some five or six weeks. Four days before admission the patient complained of dull pain throughout the abdomen, which gradually became localized to the right iliac fossa. Upon admission the temperature was 99° F., pulse 94, and respirations 24. Leukocytic count, 12,800. There was rigidity of the right rectus muscle and tenderness localized to the right iliac fossa. The appendix was removed and convalescence was uninterrupted until the sixth or seventh day, when the temperature began to rise. The fever was not accounted for until several days later, when a palpable spleen and a positive Widal reaction suggested typhoid fever. The patient was transferred to Dr. Stengel's ward, where she passed through a typical uncomplicated case of typhoid fever from which she eventually recovered.



Temperature chart of case of appendicitis as forerunner of typhoid fever.

Strangulated Meckel's Diverticulum. In 1893 I reported, with Dr. Joseph Sailer, a case of this description complicating typhoid fever. This case seems to be quite unique, since no reference to a similar experience has been found in literature either before or since. Prior to the appearance of the first symptom there was nothing to suggest any unusual condition within the abdominal cavity. About the end of the fourth week of the fever the patient suddenly complained of pain in the abdomen, referred to a point to the right of the umbilicus, and there was a slight bulging of the abdominal wall at this point—tympany on percussion and tenderness on pressure. From the time of the first pain until the operation, twenty-three hours later, we noted a fall in temperature, slight increase in pulse, a fall in the leukocytes from 10,000 to 5000, with signs of beginning general peritonitis. Exploration showed a strangulated Meckel's diverticulum with three twists, the end of which was attached to the abdominal wall.

Meckel's diverticulum occurs in about 2 per cent. of cases;

it contains Lieberkühn's follicles, and, also, often a Peyer patch, and in the majority of cases the end of the diverticulum is free, but often the end is attached to the umbilicus or, as in my own case, to the abdominal parietes in the neighborhood of the umbilicus.

Volvulus of Meckel's diverticulum is itself a very unusual condition, and as a complication of typhoid fever has never been recorded. In Sir Frederick Treves' classic work on *Intestinal Obstruction*, mention is made of but 1 case. The intestinal end of the diverticulum showed, in his as in my case, some three turns and was thus rendered impervious. It appeared, however, in this case, that there was a congenital stricture of the ileum. Sailer attributed the strangulation to the inflammation of the diverticulum, the inflammatory process having caused enough swelling of the diverticulum to tighten the twists and produce complete strangulation.

While perforation was, of course, uppermost in our minds and those of a number of the members of the staff who saw him in consultation, it seemed to all improbable. The absence at first of any signs of peritoneal irritation, the maintenance of the pulse rate, the absence of any sudden alteration in temperature, were not very suggestive. The early and significant symptoms were the period of collapse, which may attend the onset of any grave abdominal lesion, the slight swelling just to the right of the umbilicus, which was tympanitic on percussion and painful to pressure, and the fall in the leukocytes from 10,000 to 5000. That the swelling must have been a portion of the intestinal tract was evident because it was tympanitic and must have contained air; it must have been fixed, otherwise it would have varied in position. The localized tenderness at a fixed point, the slight swelling, and persistent tympany were noted on examination, but the existence of a strangulated Meckel's diverticulum was not suspected. The later symptoms were those of peritonitis, from which the patient eventually died.

Sailer and Frazier (Univ. of Penna. Medical Bulletin, 1903). F. B., aged twenty-six years. Admitted to the University Hospital on the service of Dr. John H. Musser, April 3, 1903. One year prior to admission he had had an attack which had been diagnosticated as gallstones. There was a positive Widal reaction. Physical examination on admission noted that there was still tenderness in the right iliac fossa and in the epigastrium. Twenty days after his admission, about the fourth week of the disease at 3 P.M., the patient suddenly complained of severe pain in the abdomen. The pulse was weak but not increased in rate. At 8 P.M. he was comparatively comfortable, but complained of slight pain in the region of the umbilicus. The abdomen was slightly distended just to the right of the umbilicus. There was a prominence which gave a slight sense of resistance. Percussion at this point gave a normal tympanitic note, and pressure produced slight pain. There were no signs of general peritonitis. At 5 P.M. the leukocytosis was 17,000 and at 11 P.M. it was 10,000. The nature of the condition was not clear and the patient was given a small hypodermic injection of morphine. He improved considerably; the pulse was not increased in frequency and was considerably stronger. The following morning the pulse increased to 118 and temperature had fallen to 98° F., but in the course of two hours it rose to 101°. The leukocytes were 5000. At 2 P.M. in the afternoon, twenty-three hours after the onset of pain, I was asked to see the case in consultation. At this time the abdomen was moderately distended, there was general rigidity, more marked on the right side. The prominence to the right of the umbilicus was still present and on pressure it elicited considerable pain. There was, however, superficial tenderness over the entire abdomen and the peristaltic sounds, though audible, were feeble and less frequent. There was but slight diaphragmatic respiration; breathing was almost entirely costal. The patient was vomiting at intervals dark, yellowish material; pulse, 102; respirations, 30; temperature, 99.4° F. It was quite evident that the patient had peritonitis, but the nature or origin of it seemed absolutely obscure.

The operation discovered a strangulated Meckel's diverticulum, the distended portion of which was about the size of a moderately distended gall-bladder; it was adherent to the parietal peritoneum at the point where the tenderness had been elicited. Between the distended portion and the bowel there were four twists, giving to the diverticulum the appearance of the umbilical cord. The condition was evidently one not of recent formation, as the tissue binding the diverticulum to the parietal peritoneum was fully organized. The subsequent history of the case from the time of the operation until the death of the patient, eighteen hours later, led one to believe the patient died of peritonitis rather than shock. The autopsy made by Dr. Yates showed an acute fibrinopurulent peritonitis, acute enterocolitis (typhoidal), cloudy swelling of the liver and kidneys, acute splenic tumor, and hemorrhage into the mesenteric lymph glands.

Typhoid Pancreatitis. Considering how frequently the Eberth bacillus is found in the bile, and the biliary passages affected both during and after typhoid fever, one would not be surprised to find pancreatitis more or less often as a sequel. But the case of pancreatitis reported by Moynihan, of Leeds, is the first, we believe, in which an inflammation of the pancreas due to typhoid fever has been recognized. The patient, aged thirteen years, had typhoid fever about eighteen months before. Ever since his convalescence he had more or less frequent attacks of pain in the upper part of the abdomen, continuous, accompanied by nausea, rarely by vomiting. For the past six months he had jaundice of varying intensity; there had been no chills or fever; he was considerably emaciated. On examination no tumor could be felt, but there was marked tenderness in the region above the umbilicus

and the case was regarded as one of cholecystitis, with a stone in the common duct.

Operation: Cholecystotomy. There were no stones in the biliary passages, nor any adhesions to or about the gall-bladder. The head and neck of the body of the pancreas was *twice its natural size and almost as hard as stone.* The common duct was buried in the inflammatory tissue, thus accounting for the jaundice. Typhoid bacilli were found in the bile three or four weeks after the operation. The patient's blood gave a positive Widal reaction. In 13 cases of chronic pancreatitis, Moynihan had never observed so gross an alteration in size and consistency of the gland.

Fecal Impaction. It would not be amiss to include fecal impaction among the conditions which may simulate grave abdominal lesions in typhoid fever. This subject seems to have been given little if any attention in papers and text-books on typhoid fever. The majority of cases appear to occur in childhood. Thus Miller (*Archives of Pediatrics*, 1906, vol. xxiii) reports 2 cases occurring in children whose respective ages were twelve and ten years and refers to Henry's 4 cases in which 2 were in the seventh, 1 in the twelfth, and 1 in the fifteenth year (*American Journal of the Medical Sciences*, 1902, vol. cxxiv, N. S.). In the first of Miller's cases the child had been sitting up in bed four days when it was suddenly seized with severe abdominal pains extending over the whole abdomen; simultaneously there was a rise in temperature to 102° F., the pulse from 72 to 140, and respirations from 16 to 28. There was apparent rigidity of the right rectus, pain localized to the right iliac region, marked leukocytosis (13,600). Shortly after the onset there was an almost continuous and liquid diarrhea. Examination of the rectum found it filled with hard, scyballous, fecal masses. At one time the case was thought to be acute appendicitis. As soon as the bowel was relieved of its contents the symptoms disappeared.

In the second case the symptoms were more severe; twelve days after the temperature became normal the patient, a boy of ten, complained of severe abdominal pains, tenderness was universal, but more marked over the cecum. There was no rigidity and only slight distention. Vomiting was frequent and severe. There was a rapid rise in the temperature, pulse, and respiration. The expression became anxious and the extremities cold. The leukocytes were 28,000. As in the first case a liquid diarrhea rapidly ensued. Rectal examination revealed a large fecal mass almost completely occluding the bowel.

In both these cases the almost continuous liquid diarrhea aroused suspicion as to the nature of the lesion, since it is an almost constant symptom of fecal impaction, but the abruptness of the attack in these cases, the severity of the symptoms, and the leukocytosis were quite enough to make one apprehensive of the development of an intra-abdominal lesion very much more serious in its consequences. In one of the cases the leukocytes ran 28,000. Miller attributes this to the well-known sensitiveness of the blood in children and to the fact that enteritis and colitis in early life are usually attended with a leukocytosis of from 15,000 to 30,000. Two lessons may be drawn from these cases: First, that leukocytosis in children is of little significance, in real or apparent instances of serious abdominal trouble, as it may be quite marked even when no active inflammation is present. Secondly, that a liquid diarrhea in a person habitually constipated or following typhoid fever should excite suspicion of fecal impaction.

Peritonitis Without Perforation.[1] This complication occurs about one-third as frequently as the perforative form. Its origin may be traced in some cases to an extension of the inflammation through the base of a deep intestinal ulcer, in others to the migration of bacteria through an intestinal wall but slightly abnormal. Meteorism is a very important predisposing cause and the changes resulting from hemorrhage in the wall of the intestine may favor the transmigration of bacteria. Fitz (*Trans. Assoc. Amer. Physicians*, vol. vi, p. 265) includes among the specific causes intestinal obstruction, ruptured mesenteric glands, abscess in the wall of the urinary bladder, in the ovaries and tubes, in the abdominal parietes and liver.

In the 19 cases collected by Yates he found the average age was twenty-one, the oldest fifty, and the youngest six; 8 were males and 6 females; the symptoms developed at the end of the third week, the earliest in the tenth, and the latest in the thirty-sixth day. In a case reported by Marchisin the peritonitis developed before ulceration had commenced, during the first week of the fever, thus showing the possibility of bacteria migrating through the wall in the absence of any destruction of the continuity of the mucosa. It is rather interesting to note that in the majority of these cases the fever was of the severe type. As to the symptomatology in 11 out of 14 cases the onset was acute; abdominal pain was the most constant symptom, sometimes general or profuse, but more often referred to the right side. Rigidity was commonly present. The temperature either rose or fell, and the pulse rate followed somewhat the temperature curve. In no case in which the leukocytes were counted did they exceed 12,000.

As illustrating this complication I may cite a case which I was called to see in consultation a few months ago. The patient, a young man aged twenty-four years, was under treatment for typhoid fever in the University Hospital. The case was one of moderate severity, there had been no complications; on the morning of the nineteenth day at about 6.30 A.M., he had very severe and sudden pain in his abdomen,

[1] The reader is referred to the admirable article on non-perforative peritonitis by Yates, American Medicine, May 2, 1905.

followed by vomiting. At 7.30 A.M. he felt a little better; the pain was not so severe and was diffuse in character. There was also considerable tenderness all over the abdomen, though it seemed to be rather more marked on the right side; there was some slight distention. The leukocytes numbered 8700. When I saw him at noon there was practically no change in the general condition; his temperature, which had arisen from 99° at 9.30 P.M. to 104° at 9 A.M., had begun to fall and his pulse was only 100. Upon examination I found but moderate rigidity of the abdominal parietes, more marked on the right side; moderate distention; no dulness in the flanks; some tenderness all over the abdomen, but decidedly more acute in the right iliac fossa. In view of the suddenness of attack, the sudden sharp pain, the vomiting, followed by signs of general peritoneal irritation, I suspected perforation and advised operation. Dr. Stengel, under whose care the patient was, had arrived at a similar conclusion and the patient was prepared at once for operation. Upon opening the abdomen through a right rectus incision no air escaped, but there was a gush of turbid fluid. The ileum was red and sticky, as though it had been scalded; a hurried inspection beginning at the cecum found, about ten inches from the ileocecal valve, an area of induration in the ileum about the size of a quarter, evidently the base of an ulcer. There were, however, no signs of perforation either at that or any other point. Fearing that the peritonitis might have been due to leakage through the base of this ulcer, it was covered with a patch of omentum; a pelvic drain was introduced and the wound closed. The operation lasted twenty minutes and the patient left the table in excellent condition. For the first thirty-six hours there were no untoward symptoms, but from that time on he very rapidly grew worse and died twelve hours later.

In this as in all the other reported cases there were no clinical features of non-perforative peritonitis to distinguish it from perforation, and as a matter of fact in all but 2 cases, which were thought to be appendicitis, a diagnosis of perforation was made. As Fitz well says, "the so-called symptoms of perforation merely indicate the beginning of a peritonitis and may be present as the result of other local causes of peritonitis in typhoid fever than a perforative enteritis."

From the cultures, which have been made at operation and postmortem, it is more likely that the infection is due to the typhoid bacillus; resulting inflammation may be of the serous, serofibrinous, or purulent type. The prognosis is always grave; out of a series of 23 cases (20 collected by Yates) 14 were operated upon and 5 recovered, but all of the unoperated cases died. The principles governing the treatment and the indications for operation do not differ materially from those of perforation. Inasmuch as the two are practically indistinguishable, it is impossible to determine before operation whether or not there is a perforation. The operation must be in the nature of an exploration and in each case should consist in a rapid inspection of that portion of the bowel in which perforation most commonly occurs. Failing to find any, the subsequent steps will depend somewhat upon the judgment of the operator. An enterostomy might be considered expedient in cases of grave meteorism, although it is doubtful whether, in view of the fact that a considerable section of the bowel may be paralyzed, the introduction of a tube would have any effect other than to drain a very limited segment. At the conclusion of the operation a drainage tube should be introduced into the pelvis.

A word or two may not be out of place with reference to the subsequent or after-treatment of all cases of typhoid fever requiring a celiotomy and drainage. The mortality is so discouragingly high that the greatest attention should be paid to detail in the management of the case throughout. In peritonitis of other origin the prescribed treatment would consist in the withdrawal of all nutrition by mouth, in continuous enterocylsis by the Murphy method, and in placing the patient in the Fowler position. The propriety of placing typhoid subjects in the Fowler position may well be questioned. Dr. J. Alison Scott regards it as at least a very questionable procedure, and I am inclined to agree with him. Under no other condition would typhoid-fever patients be allowed to sit up in the active stage of the disease, and in cases of peritonitis, with or without drainage, the favorable influence of posture upon the drainage may be more than counter-balanced by its unfavorable influence upon the circulation. There are no practical or theoretical objections to enteroclysis; in the question of diet, however, we must again recognize a distinction between cases of peritonitis of sudden onset and those coming on in the course of an exhausting infectious disease. In the latter instance nutrition cannot be withheld for two, three, or four days without seriously jeopardizing the patient's condition. Moderate amounts of liquid nourishment should be given as soon as the patient has recovered from the immediate effects of the operation, possibly not longer than twelve hours, and may be supplemented by nutritive enemata.

THE EXISTENCE OF AN ANTI-ENZYME IN TAPEWORM.

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(From the Robert Hare Laboratory of Chemistry.)

The question why does not the living stomach, intestines, and the host of worms which thrive in the intestinal tract undergo digestion is usually answered, that they normally secrete an antibody which overcomes the activity of the enzymes. Whether these antibodies have been isolated or not, their existence is generally conceded.

That the living Tænia saginata (beef tapeworm) secretes such an anti-enzyme appears to be shown by the experiments detailed in this paper.

The worm, measuring ten feet in length, was obtained alive from a student of the University of Pennsylvania.

A few minutes after its passage from the rectum a portion was divided into parts made up of four segments each, which were placed in separate test tubes previously prepared as will be described in the experiments. The remaining portion of the living worm was finely ground in a mortar with clean sand, glycerin was added, and the mass was allowed to stand, being thoroughly stirred once daily, during a period of eight days. The mass was then placed on a filter of washed and moistened muslin, and the glycerin filtrate was employed in the experiments which will be subsequently described.

Fluid expressed by pressure from segments of the worm and filtered through washed and moistened muslin responded to the biuret reaction, and produced a slight reduction of Fehling's solution.

All references to the biuret reactions and Fehling's test in the experiments are only considered of value when the results obtained were more marked than those obtained with the fluid expressed by pressure from the worm.

The fibrin employed in the experiments was obtained from ox-blood and was preserved in glycerin, and when used in the experiments the greater part of the glycerin was removed by pressing the mass of fibrin. The mass of fibrin used in each experiment was of the size of a small pea.

EXPERIMENTS.

All of the experiments were made in a digesting oven at a temperature between 37° C. and 40° C. and the progress of digestion was noted every hour for the first twelve hours and afterward at the expiration of several hours.

Series A. Into each of several test tubes was placed 10 c.c. of 0.2 per cent. hydrochloric acid, 2 drops of toluene, and 4 segments of live worm.

Tube No. 1 contained acid, toluene, and worm only. The first evidence of change in the worm occurred after the expiration of two days. A slow thinning of the segments took place until at the end of the fourth day about three-fourths of the worm had disappeared. The resulting solution gave a decided biuret reaction.

Tube No. 2 contained acid, toluene, worm, and fibrin. In this tube the results were similar to tube No. 1, the fibrin undergoing change similar to that of the worm.

Tube No. 3 contained acid, toluene, worm, and pepsin. In this case twenty-four hours elapsed before any evidence of action upon the worm took place, and after the expiration of three days only a very small quantity of finely divided solid remained. The filtered fluid gave a decided response to the biuret reaction.

Tube No. 4 contained acid, toluene, worm, pepsin, and fibrin. The results were identical with tube No. 3, the fibrin showing changes similar to that of the worm.

Tube No. 5 contained acid, toluene, worm, and caroid (papain). After twenty-four hours had elapsed signs of separation of the segments with slight swelling appeared. At the end of the third day the segments were completely separated with but slight change in the structure of each segment. The filtered fluid responded slightly to the biuret reaction.

Tube No. 6 contained acid, toluene, worm, caroid (papain), and fibrin. The first signs of digestion of the fibrin occurred after twenty-four hours had elapsed, and it was completely digested at the end of the third day. The worm showed the same changes as in tube No. 5. The biuret test with the filtered fluid showed a more marked reaction than with the fluid of tube No. 5.

Series B. The tubes in this series contained 10 c.c. of a 0.5 per cent. sodium carbonate solution, 2 drops of toluene, and 4 segments of live worm.

Tube No. 1 contained sodium carbonate, toluene, and worm only. The results of this tube were lost.

Tube No. 2 contained sodium carbonate, toluene, worm, and extract of pancreas. The first evidence of action upon the worm appeared in thirty-six hours. At the end of the third day only a small quantity of finely divided worm remained. The biuret reaction applied to the filtered fluid gave a decided result.

Tube No. 3 contained sodium carbonate, toluene, worm, fibrin, and extract of pancreas. The results were identical

with those of tube No. 2. The fibrin exhibited the first evidence of digestion in thirty-six hours and completely disappeared at the end of the third day.

Tube No. 4 contained sodium carbonate, toluene, worm, fibrin, and caroid (papain). The first evidence of any change in the fibrin was shown in twenty-four hours. The fibrin completely disappeared at the end of the third day. The worm remained intact, showing little change after the expiration of four days. The filtered fluid gave a decided response to the biuret test.

Tube No. 5 contained sodium carbonate, toluene, worm, fibrin, and diastase. The fibrin showed the first sign of change after two days, slowly splitting into fine shreds which remained after the expiration of the fourth day. The worm remained intact, showing very little change at the end of the fourth day. The filtered fluid responded faintly to the biuret reaction.

Series C. In this series the tubes contained 10 c.c. of a 0.5 per cent. sodium carbonate solution, 2 drops of toluene, 4 segments of live worm, and 1 c.c. of a 0.5 solution of starch.

Tube No. 1 contained sodium carbonate, toluene, worm, starch, and diastase. The starch was changed into sugar in two hours. The worm remained intact three days, after which time the filtered fluid gave a faint response to the biuret test, and a decided response to Fehling's test.

Tube No. 2 contained sodium carbonate, toluene, worm, starch, and extract of pancreas. Results identical with those in tube No. 1 were obtained, except that the worm was digested in three days, leaving only a very slight quantity of solid tissue in a finely divided condition. The filtered fluid gave a decided response to the biuret reaction.

Tube No. 3 contained sodium carbonate, toluene, worm, starch, and pepsin. The starch was converted into erythrodextrin in six hours, but no sugar could be found by various tests. This condition remained unchanged three days. No tests were made after the third day. A faint response to the biuret test was obtained after the third day, the worm having remained intact.

Tube No. 4 contained sodium carbonate, toluene, worm, starch, and caroid (papain). The results were identical with tube No. 3.

Series D. In this and the following series, instead of segments of the live worm, 1 c.c. of a glycerin extract of the worm was employed together with 10 c.c. of 0.2 per cent. hydrochloric acid, 2 drops of toluene, and a mass of fibrin the size of a small pea.

Tube No. 1 contained as stated above. Only a slight thinning of the fibrin occurred in twenty-four hours.

Tube No. 2 contained as stated above, with pepsin. The fibrin was completely digested in ten hours.

Tube No. 3 contained as stated above, with caroid (papain). Only a slight quantity of the fibrin was digested in twenty-four hours.

Tube No. 4 contained as stated above, with diastase. No change occurred in the fibrin in twenty-four hours.

Series E. Each tube of this series contained 1 c.c. of a glycerin extract of the worm, 10 c.c. of a 0.5 per cent. sodium carbonate solution, 2 drops of toluene and fibrin.

Tube No. 1 contained as stated above. No change took place in the fibrin in twenty-four hours.

Tube No. 2 contained as stated above, with extract of pancreas. The first signs of action on the fibrin were observed in eight hours. The fibrin was completely digested in twenty-four hours.

Tube No. 3 contained as stated above, with caroid (papain). Only a slight change in the fibrin was observed in twenty-four hours.

Tube No. 4 contained as stated above, with diastase. No change in the fibrin was observed in twenty-four hours.

Series F. In this series each tube contained 1 c.c. of a glycerin extract of the worm, 2 drops of toluene, and 1 c.c. of a 0.5 per cent. solution of starch.

Tube No. 1 contained as stated above. The starch was completely transformed into sugar in one hour.

Tube No. 2 contained as stated above, with diastase. The presence of the diastase did not hasten the transformation of the starch into sugar as compared with tube No. 1.

Tube No. 3 contained as stated above, with diastase and 10 c.c. of a 0.5 per cent. sodium carbonate solution. The same length of time (one hour) was required for complete conversion of the starch into sugar as in tube No. 1.

Tube No. 4 contained as stated above, with extract of pancreas. The conversion of the starch into sugar occurred in one hour.

Tube No. 5 contained as stated above, with extract of pancreas and 10 c.c. of a 0.5 per cent. sodium carbonate solution. Identically the same length of time (one hour) was required for complete hydrolyzation of the starch as in tube No. 1.

CONTROL EXPERIMENTS.

Tube No. 1 contained 10 c.c. of 0.2 per cent. hydrochloric acid, 2 drops of toluene, fibrin, and pepsin.

Tube No. 2 contained 10 c.c. of a 0.5 per cent. sodium carbonate solution, 2 drops of toluene, fibrin, and extract of pancreas.

Tube No. 3 contained the same as tube No. 2 except caroid (papain) instead of extract of pancreas. The fibrin in all of these tubes was completely digested in six hours.

Tube No 4 contained 10 c.c. of a 0.5 per cent. sodium carbonate solution, 2 drops of toluene, 1 c.c. of a 0.5 per cent. starch solution, and extract of pancreas.

Tube No. 5 contained the same as tube No. 4 except diastase instead of extract of pancreas.

Tube No. 6 contained the same as tube No. 4 except caroid (papain) instead of extract of pancreas. The starch in each tube was completely hydrolyzed in one hour.

It will be seen from the experiments that the glycerin extract of the worm had no influence upon the activity of the enzymes upon starch, that the segments of the live worm retarded the action of the enzymes upon starch, two hours being required for complete hydrolysis; whereas, the same quantity of starch in the control experiments required only one-half that length of time, and that segments of the live worm and also a glycerin extract of the worm retard the action of the enzymes upon fibrin.

Under normal conditions, as shown by the control experiments, complete digestion of fibrin took place in six hours, whereas from ten hours to several days were required in the presence of the live worm or of its glycerin extract.

From the results of these experiments it appears that the tapeworm secretes an anti-enzyme.

IMPERFORATION OF THE RECTUM AND ANUS.

WITH A REPORT OF 12 CASES FROM THE CHILDREN'S HOSPITAL OF PHILADELPHIA, AND AN ANALYSIS OF 95 RECENT OPERATIONS.

By Astley Paston Cooper Ashhurst, M.D.,

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Imperforate rectum, a congenital malformation which is said to occur only once in about ten thousand births, is, nevertheless, encountered sufficiently often to make its diagnosis and treatment of immense practical importance. Of the 12 patients who have been treated for this condition at the Children's Hospital since its foundation in 1855, no less than 11 have been operated on during the last decade. A brief report of these cases follows:

Case 1.—1879. Joseph C., aged three days; admitted July 29, for imperforate rectum. Left lumbar colotomy done. Died in 24 hours.

Case 2.—1896. Edward C., aged one day; one of twins; admitted June 15th. After failing to find rectum by perineal incision, Dr. H. R. Wharton did left iliac colotomy. Died four days later.

Case 3. 1896. Hattie C., aged six hours; admitted August 6th.; operation by Dr. R. G. Le Conte. After failure to find rectum by incision in perineum, left lumbar colotomy was done. The jaundice, present on admission, deepened, and death occurred four days later.

Case 4. 1896. Rebecca E., aged twelve weeks; operation by Dr. John Ashhurst, Jr., November 25th. The rectum opened into the vagina low down. The perineum was incised over the normal site of the anus, the rectum opened and sutured to the skin. Recovered.

Case 5.—1897. Anna W., aged seven weeks; operation by Dr. John Ashhurst, Jr., December 15th. Bowels have moved three or four times daily since birth, with straining and pain. Proctodeum absent; a small sinus running up from fourchette to rectum. The feces are discharged through this sinus, which is in the form of a goose-quill. A sound was passed up the sinus, its point made to impinge on normal site of anus; incision made on point of sound, rectum opened, mucous membrane sutured to skin with silk. Patient was discharged three weeks later with excellent sphincter action; the vaginal sinus had closed.

Case 6.—1899. Lola C., aged one month; operation by Dr. Samuel Ashhurst, April 18th. The rectum opened into vagina low down. Same operation as in Case 5. Recovered.

Case 7.—1900. Amelia M., aged three days; operation by Dr. H. R. Wharton, October 26th. Child had been born by breech presentation, in easy labor. A little meconium was noticed on diaper the next morning, being supposed to come from anus. Examination showed the proctodeum present, but occluded at depth of one-half inch. Perineal incision failed to find rectum; vagina accidentally punctured. Perineal wound packed, and left iliac colotomy done. There were several drams of clear, straw-colored fluid in the peritoneal cavity, so a gauze drain was inserted in the abdominal wound just above the false anus. There was an abundant escape of meconium on opening the gut. The child's mother refused to nurse it at home, so it was kept in the hospital, and finally died of malnutrition on December 8, 1900, just six weeks after the operation. The iliac anus acted well until death.

Case 8.—1901. William C., aged five days; operation by Dr. J. P. Hutchinson, August 18th. Proctodeum was one-quarter of an inch deep. There was omphalitis. The abdomen was distended and tympanitic. Peristalsis was evident. Vomiting. Hemoglobin, 92 per cent.; white blood corpuscles 19,800; red blood corpuscles 5,448,000. After etherization, and with a sound in the bladder, a crucial

incision was made in the perineum. The rectum could not be found. The umbilicus was covered with collodion, and the left iliac region of the abdomen opened. There was a gush of scropurulent fluid on opening the peritoneum. The colon, which was dark and unhealthy, was drawn into the wound and opened. There was a profuse discharge of dark, tarry feces. The bowel was washed out with sterile water, and a false anus established. The child died nine hours later.

Case 9.—1901. Charles D., aged three days; operation by Dr. R. G. Le Conte, September 4th. The family physician had made an incision in the perineal region, but no rectum was found. The abdomen on admission was much distended, very hard, dark, and covered with enlarged veins. One-quarter of an inch below the root of penis was a pinhole opening through which some meconium had leaked. A probe introduced here passed upward and backward nearly two inches toward sacro-iliac joint, where a membranous resistance was encountered. An incision in the perineum, with this probe as a guide, was made, and the rectum opened. The child died twenty-four hours later.

Case 10.—1903. Mary M., aged nine months; operation by Dr. H. R. Wharton, November 26th. No abnormality had been noted by parents until one month ago, when, as a result of weaning and eating table food, the child became constipated. Examination showed that the anus was absent, and that the rectum opened into the vulvar orifice just within the fourchette. Under ether narcosis, the rectal pouch was exposed by dissection in the perineum, sutured to the skin, and opened. The mucous membrane was then sutured to the margin of the skin. The child did well and was discharged over two weeks later in good condition.

Case 11.—1906. Valentine B., aged one day; operation by Dr. A. P. C. Ashhurst, July 30th. Patient was the elder of twins. Early this morning, when grandmother changed diaper of brother, she examined this baby also, and found there was no anus. The family physician was called, and made a puncture, but no meconium was discharged, and baby was sent to hospital. The baby was vomiting, and was slightly jaundiced. The perineal raphe was normal, but at the site of anus was a prominent button of skin, with small depression in centre, not large enough to lodge a probe. The perineum felt distended. No anesthetic was administered; with the baby lying on a hot-water bag, and held in the lithotomy position, a median incision one inch long was made, and deepened through the cellular tissue for over an inch and one-half, when a bulging pouch the color of meconium was discovered. This was punctured, and the puncture dilated with hemostatic forceps; five or six ounces of meconium were then discharged in the course of one-quarter of an hour. When the discharge ceased, the rectum was sutured to the skin of the anus by four catgut sutures, the bowel being dilated by the fingers as much as possible. Time of operation thirty minutes. The child was sent home in an hour or so, and reported next day to the dispensary. He had had two normal movements in the interval; progress was uneventful. A streak of blood was noticed in movement on August 20th. On September 18th, seen again; the twin had died of pneumonia, but this baby had survived a sharp attack of bronchitis. Bowels move normally. On January 12th there was some constipation, and the anus was dilated by Dr. Hodge at the hospital dispensary. On May 14th I saw the patient again; he had been constipated, but a finger passed up the bowel felt no stricture, only a very well-developed sphincter. No further trouble has been experienced.[1]

Case 12.—1906. Lincoln J., aged two days; operation by Dr. E. H. Siter, October 16th. Family physician had made an incision in the perineum, but had not found the rectum. Operation under ether: an incision in perineum one inch and one-half deep was made, but rectum was not found. Then a left iliac incision was made, and the peritoneum opened; many coils of small bowel were forced out and were replaced with difficulty. Colon could not be found. A coil of small intestine was opened and sutured to the abdominal wound. No meconium was discharged. Time of operation, two hours. Some meconium was passed from the urethra after the operation, but none from the false anus. Jaundice developed, and death occurred fifteen hours after operation.

To these 12 cases may be added the records of 83 collected from surgical literature since 1900, giving a total of 95 operations:

Stiedа's classification.	Cases.	Recovered.	Died.	Mortality per cent.
I. Atresia ani seu recti congenita simplex:				
1. Atresia ani simplex (anus absent)	27	21	6	22.2
2. Atresia recti simplex (anus present)	16	8	8	50.0
3. Atresia ani et recti (both absent)	16	2	14	87.5
II. Atresia ani s. recti complicata cum communicationibus:				
1. Atresia ani et communicatio recti cum vagina	9	8	1	11.1
2. Atresia ani et communicatio recti cum vesica urinaria	6	3	3	50.0
3. Atresia ani et communicatio recti cum parte prostatica urethræ	4	2	2	50.0
III. Atresia ani s. recti complicata cum fistulis:				
1. Atresia ani cum fistula perineali	4	3	1	25.0
2. Atresia ani cum fistula scrotali	0	0	0	00.0
3. Atresia ani cum fistula suburethrali:				
(a) cum fistula penali	2	2	0	00.0
(b) cum fistula intraprœputiali	0	0	0	00.0
(c) cum fistula extraprœputiali	2	1	1	50.0
4. Atresia ani cum fistula vestibulari	9	8	1	11.0
Total	95	58	37	39.0

The most important classification, so far as treatment is concerned, is into those patients with absolute occlusion of the rectal canal, and those in whom there exists some form of

[1] I take this opportunity to thank Dr. Hutchinson for the privilege of operating on and reporting this case.

fistulous exit for the meconium. The former class requires immediate operation to avert death from obstruction; whereas, patients in the latter class sometimes live a considerable time before the abnormality is even known to exist. Of the more elaborate classifications, that of Stieda (*Archiv f. klin. Chir.*, 1903, lxx, 555) seems to me the best for practical purposes, and will probably in time entirely supercede that of Bodenhamer, which is still widely quoted. The frequency of the various forms of malformation, in the present series of 95 cases, may be seen in the preceding table.

The prime object of treatment, of course, is to form an opening for the occluded bowel, if possible in the region of the proctodeum. If this proves impossible, the usually accepted course is to perform Littré's operation of left iliac colotomy; and when the patient reaches a suitable age, it is then recognized as proper to attempt to establish a communication between the blind end of the rectum and the perineum, the manipulations now being aided by the introduction of a probe through the iliac anus. As will be seen from the cases herewith reported, it is quite unusual for patients who have been subjected to iliac colotomy to survive long enough for any such attempt to be made. If the infant is not already so feeble, from delay in resorting to operation, as to die within a few hours after its performance, death almost invariably ensues within a few weeks or months from malnutrition or exhaustion. Moreover, the question of the possibility or impossibility of reaching the rectal pouch from below is largely a personal one with the individual surgeon who does the operation. One surgeon will become faint-hearted as soon as the skin has been incised and will at once resort to colotomy; while another, with a little more persistence, will successfully reach the rectal pouch through the perineum, and will thus spare his patient the very much greater risk of an abdominal operation. And this is quite apart from the question of the actual depth at which the rectum is found. Many cases are on record where the operator found it quite impossible to discover the rectum from below, while at autopsy only a few hours later its mucous lining was proved to be only an inch or even less from the skin of the perineum. Moreover, Bodenhamer's very extensive researches showed (*New York Med. Journal*, 1889, xlix, 562) that the cases where the rectum and colon were totally absent formed a very small proportion of the whole, only 41 out of 465 cases which he studied; so that the chances are altogether in favor of the perineal search being successful, if not abandoned needlessly soon.

There appears to have been no statistical study of these operations since 1893, when Anders (*Archiv f. klin. Chir.*, 1893, xlv, 489) published an analysis of 100 cases; and it was with some idea of making clear to my own mind the present-day results of the various operations that the following study was undertaken, for I am firmly convinced that the surgeon, unless he is thoroughly well aware beforehand of the merits and demerits of the numerous operations now currently employed, and of the frequency with which the rectum may be reached from below, will too soon abandon the safer if more tedious procedure, for one that is brilliant in its execution but less sure in its results.

The operations, and their results, in the 95 cases now under discussion, may be seen in the annexed table.

Operation.	Primary statistics.				Improved statistics.			
	Cases	R.	D.	Mortality %	Cases	R.	D.	Mortality %
Perineal puncture	2	2	00	00.0	2	2	0	00.0
Perineal incision	7	2	5	71.4	3	2	1	33.3
Perineal proctoplasty	33	26	7	21.2	30	26	4	13.3
Perineal proctoplasty (for atresia ani vaginalis s. vulvaris)	12	11	1	8.33	11	11	0	00.0
Rizzoli's operation[1]	5	5	00	00.0	5	5	0	00.0
Primary left iliac colotomy	14	5	9	64.3	14	5	9	64.3
Secondary left iliac colotomy	15	4	11	73.3	13	4	9	69.2
Secondary left lumbar colotomy	2	00	2	100.0	2	00	2	100.0
Primary laparotomy with secondary perineal proctoplasty	2	1	1	50.0	2	1	1	50.0
Secondary laparotomy with tertiary perineal proctoplasty	3	2	1	33.3	3	2	1	33.3
	95	58	37	39.0	85	58	27	31.7

The so-called "improved" statistics have been obtained by excluding from the whole number 10 cases, all fatal, in none of which did the operation have any bearing on the patient's death. The cases thus excluded are the following:

From the statistics of perineal incision 4 cases are excluded. (1) Doussan's patient, whose parents refused colotomy when the rectum could not be found in the perineum. The child might have survived colotomy, and it is evidently unfair to charge its death to the perineal incision. (2) Eustache's patient, in whom operation was abandoned because there was found to be imperforation of the esophagus, which would have caused a fatal termination even if the rectal imperforation had been successfully overcome. (3) Günther's seventh patient, in whom the perineal operation was abandoned without finding the rectum, and the child left to die without further interference. (4) Wanous' patient, in whom the same series of events took place. It is evidently unfair to charge these deaths up against perineal incision, when the bowel was not reached; an incision on the buttock would have had quite as much therapeutic value.

From the statistics of perineal proctoplasty 3 cases may be excluded: (1) Edington's patient, in whom, although the rectum was successfully opened at a depth of only one inch, death occurred ten days later from cellulitis, and at autopsy it

[1] Rizzoli ("Tre Casi di Atresia Congenita dell' Ano." Bologna, 1866), instead of merely opening the rectum from the perineum, in cases of atresia ani vaginalis, transplanted the vaginal opening of the rectum to the normal site of the anus, and then repaired the posterior vaginal wall. His first operation was done in 1856, but the original reference (Mem. Accad. Sc. di. Bologna, 1856 57) has not been accessible to me.

was found that only one kidney existed. (2) Udall's patient, in whom at autopsy there was found agenesis of part of the jejunum and other malformations which would have caused death even if there had been no anorectal imperforation. (3) Trautner's patient, in whom death was due to imperforation of the esophagus.

From the statistics of perineal proctoplasty for atresia ani vulvaris may be excluded Stevens' case, in which death occurred four days after a simple perineal operation, from symptoms strongly suggestive of imperforation of the esophagus, although this is not mentioned by Stevens, who attributed the fatal termination to bronchopneumonia.

From the statistics of secondary iliac colotomy 2 cases may be excluded: (1) The case of Dieulafé and Gilles, who reported a death from imperforation of the esophagus thirty hours after operation. (2) Manton's patient, who recovered after the performance of secondary left iliac colotomy at the age of one day, and lived in health for twenty-four days, when feces first appeared in the urine. For this complication laparotomy was done; the colon was divided below the false anus and both ends closed. The child died five days later at the age of thirty days. It seems scarcely just to charge this death up to the account of iliac colotomy.

Nevertheless, the unimproved statistics are given, as well as those obtained by the omission of these doubtful cases; and the reader can be guided by the first, if he thinks these 10 cases are erroneously excluded.

Although the operation of perineal proctoplasty appears from these figures to be very much less serious than any other procedure for complete occlusion of the rectum or anus, it must be remembered that it is the simplest cases which are amenable to this treatment, and that the more serious cases demand a more dangerous operation. Perhaps the best way to obtain a just idea of this question is to consider together all those cases in which the bowel was not reached primarily by way of the perineum. There are 36 such cases (primary iliac colotomy, 14; secondary iliac colotomy, 15; secondary lumbar colotomy, 2; primary laparotomy, 2; secondary laparotomy, 3); among these patients 22 deaths occurred, a mortality of nearly 65 per cent.

Among these 36 cases, the location of the lower blind end of the rectum was subsequently determined (by operation or by autopsy) in 22 patients. In 3 of these it is probable that even the most extensive search from below would have failed to locate the blind end of the gut. These cases are the patients of Lotsch, Chalot, and Delagénière (Case 1). In the case recorded by Lotsch, Habs did laparotomy without trying a perineal incision because the urine was stained by meconium. He planned to separate the bowel from the bladder, and then to pull the rectum down through a perineal incision. This operation was successfully carried out, the child recovering with good sphincter action. In Chalot's patient, the perineal incision was abandoned when the promontory of the sacrum was reached; laparotomy then showed that the blind end of the sigmoid was 5 cm. higher still. It was successfully isolated and transplanted to the perineum, the child making an excellent recovery. In Delagénière's first case the perineal incision was abandoned, and then laparotomy showed that the bowel was too high to be reached from below. It was successfully transplanted to the perineum, but the child died on the ninth day.

Of the remaining 19 out of the 22 patients in whom the bowel was not primarily opened in the perineum, and in whom the exact location of the blind end of the rectum was subsequently determined by operation or autopsy, it seems probable that the rectum could have been reached from below in 8 patients, and it is practically certain that it could have been so reached in 11 patients.

Considering first the 11 patients—Deely, Delagénière (Case 3), Delèpine, Elgood, Hall, Luther, Montgomery (Cases 5, 7, 8, and 9), and Perkins—in whom it seems certain that a perineal operation should have been successful, we find that the patients of Delagénière, Delèpine, Elgood, Luther, and Montgomery (Cases 5 and 9), 6 in number, were treated by primary left iliac colotomy without any attempt being made to reach the rectum by a perineal incision. In Delagénière's patient the rectum was found only 6 cm. (2½ inches) away from the perineum, so a secondary perineal protoplasty was performed; the child died in five days. Delèpine's patient recovered, and when three months later it was determined to connect the rectum with the anus the blind end of the rectum was found only 3 cm. distant from the skin of the perineum. Elgood's patient died in four days, and it was found at autopsy that the blind end of the rectum emptied into a cloaca, which was separated from the surface of the perineum by only one-eighth of an inch; therefore, a very little patient dissection in the perineum would have opened the rectum itself, or, at least, the cloaca into which it drained. Luther's case, in which operation was done by Martin, recovered after primary iliac colotomy, and when six weeks later a perineal incision was made the lower end of the rectum was easily reached. This patient finally died at the age of three months, soon after an operation of intestinal resection done for strangulated prolapse of the bowel through the iliac anus, which had not yet closed. It is clear that if the bowel had been opened from the perineum in the first place, no such catastrophe as this would have put so gloomy an end to a brilliant series of operations. In Montgomery's 2 patients death occurred after periods of three days and four days, respectively, after primary iliac colotomy had been done; and the autopsies showed that the lower end of the rectum was distant from the perineum only three-quarters of an inch in each case.

The remaining 5 patients of those 11 in whom it seems

certain that a perineal operation should have been successful were reported by Deely, Hall, Montgomery (Cases 7 and 8), and Perkins. In Deely's patient a perineal incision was made, but abandoned at the depth of one inch; iliac colotomy was done, and the child died the next day; autopsy showed that had the incision been extended only one inch deeper the rectum would have been opened. Surely it is better to explore to a depth of two inches than to do colotomy. Hall incised the perineum to a depth of one and one-half inches, and felt a distended sac which he thought was the rectum; then he opened the abdomen in the left lumbar region, and determined that the distended sac which he had felt from below really was the blind end of the rectum. He then sutured the rectum to the skin of the perineum and opened it. His patient recovered; but one is tempted to ask whether this recovery was due more to good luck or good management. Montgomery's seventh and eighth patients died after iliac colotomy, which had been resorted to after the perineal incision had been abandoned. As autopsy showed the rectum distant only one inch and one and one-quarter inches, respectively, from the perineal surface, it is evident that his perineal dissections were not very extensive. In Perkins patient, who also died after secondary iliac colotomy, autopsy showed the rectum only one-half inch above the perineal incision, which had been abandoned at a depth of one inch.

Coming now to those patients, 8 in number, reported by Brault, Dieulafé, Kirmisson (Cases 1 and 2), Lacasse, Manton, Montgomery (Case 1), and Squires, in whom it seems *probable* but is not certain, that primary perineal proctoplasty should have been successful, we find that in 4 of these cases—Montgomery (Case 1), Kirmisson (Case 1), Lacasse, and Squires—no attempt was made to reach the bowel from below. In Montgomery's patient primary laparotomy was done; autopsy showed that the rectum was four inches distant from the skin of the perineum. In Kirmisson's patient primary colotomy was done, and six months later the rectum was easily opened from the perineum. The patient of Lacasse also was treated by primary iliac colotomy, and the next day at autopsy the rectum was found to empty into the bladder; so that it is probable that it could have been reached through the perineum. The patient of Squires died five days after primary iliac colotomy: the bowel ended at the sigmoid, but it is not impossible that it could have been reached through the perineum; at any rate the child could not have become any more dead if the perineal incision had been tried before resorting to colotomy. In the remaining four patients in this category—those of Brault, Dieulafé, Kirmisson (Case 2), and Manton—a perineal incision was made, but was abandoned, secondary iliac colotomy being done. Brault succeeded three weeks later in reaching the rectum from below by means of partial resection of the sacrum; but there is nothing to show that this form of operation would not have been equally successful if employed at birth, instead of colotomy. Unfortunately this patient died of marasmus when nearly five weeks old. The patient reported by Dieulafé and Gilles died from imperforation of the esophagus soon after secondary iliac colotomy; the autopsy showed that the bladder and rectum opened into a common sac, and there is every probability that more careful search in the perineum would have been successful in evacuating the rectum, though, of course, it could not have altered the ultimate course of events. In Kirmisson's second patient, retrograde catheterism of the rectum, through the iliac anus, showed one week after operation that the lower end of the bowel was close to the perineum, where it was then successfully opened. Manton's patient did well for twenty-five days after secondary colotomy; then, because feces appeared in the urine, laparotomy was done; the colon was divided below the false anus and both ends closed. Autopsy five days later showed that the bowel communicated with the prostatic urethra; hence it could, in all probability, have been reached from the perineum primarily had the incision been carried a little deeper.

We find, then, that, as stated on a previous page, in only 3 out of the 22 cases in which the rectum was not found by perineal incision, and which are reported in sufficient detail, would it have been impossible to reach the rectum by the lower route; that in 11, in all probability, and in 8 it certainly could have been reached by perineal incision. Among these 19 cases there are at least 8 in which the patient's death was probably due, in large measure, to the resort to a more serious operation than was necessary. The mortality of abdominal operations in these patients is nearly 65 per cent., while that of perineal proctoplasty is less than 22 per cent. Even with resection of the sacrum to facilitate the perineal search, the immediate mortality was only 21.42 per cent. among 14 such operations (1887–1899) collected by Matas (Keating's *Cyclopedia of the Diseases of Children*, vol. v; Edwards, Philadelphia, 1899, p. 767), and although only 4 of these 14 cases were reported as ultimate recoveries, yet even this is a fair showing when compared with the ultimate recoveries following iliac colotomy.

It is impossible to state in figures just what is the ultimate mortality of these various operations, because the congenital malformation may with justice be blamed for predisposing to a fatal termination; but there can be very little room for doubt that a baby with an iliac anus is much less apt to survive than is one whose bowel terminates in the anal region. This being the case, and the immediate mortality of the perineal operation being so much lower, the paramount importance of finding the rectum from the perineum cannot be overestimated.

That primary colotomy will *never* be justifiable, it ill becomes any one surgeon to say. No doubt some infants

will be encountered so nearly dead from obstruction that colotomy or enterotomy may seem proper as a euthanasial measure, or at least as more calculated to obviate the tendency to death than an incision in the perineum. But it certainly seems that, in view of the rarity of the inaccessibility of the rectum from below, as shown in the cases here analyzed, a surgeon should have very good reasons for abandoning the perineal operation.

LIST OF CASES ANALYZED.

I. ATRESIA ANI SEU RECTI SIMPLEX.

1. *Atresia Ani Simplex.*

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4. Causey. Memphis Med. Monthly, 1902, xxii, 431.
5. Cestero. Bol. de la Asoc. Méd. de Puerto Rico, 1904, ii, 273.
6. Deely. Brooklyn Med. Jour., 1904, xviii, 253.
7. Edington. Jour. of Anat. and Physiol., London, 1903–4, xxxviii, 476.
8. Ferraresi. Riforma Medica, 1902, xviii, 686. Obs. ii.
9. Ferraresi. Riforma Medica, 1902, xviii, 686. Obs. iii.
10. Ferraresi. Riforma Medica, 1902, xviii, 686. Obs. vi.
11. Gunther. Ueber Atresia Ani, Inaug. Dissert., Bonn, 1902, Fall 2.
12. Günther. Ueber Atresia Ani, Inaug. Dissert., Bonn, 1902, Fall 3.
13. Günther. Ueber Atresia Ani, Inaug. Dissert., Bonn, 1902, Fall 4.
14. Günther. Ueber Atresia Ani, Inaug. Dissert., Bonn, 1902, Fall 5.
15. Günther. Ueber Atresia Ani, Inaug. Dissert., Bonn, 1902, Fall 8.
16. Hoppe. Vereinbl. d. pfälz. Aerzte, Frankenthal, 1903, xix, 36.
17. Laurie. Lancet, 1902, i, 158. Case 2.
18. Laurie. Lancet, 1902, i, 158. Case 3.
19. Montgomery. Lancet, 1900, i, 304. Case 5.
20. Montgomery. Lancet, 1900, i, 304. Case 8.
21. Montgomery. Lancet, 1900, i, 304. Case 9.
22. Pepper. Jour. of Med. and Science, Portland, 1904–5, xi, 365.
23. Perkins. Colorado Medicine, 1903–4, i, 92.
24. Scott. Brit. Med. Jour., 1903, i, 425.
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26. Sullivan. Brooklyn Med. Jour., 1904, xviii, 253. Case 1.
27. Sullivan. Brooklyn Med. Jour., 1904, xviii, 253. Case 2.

2. *Atresia Recti Simplex.*

28. Brault. Gazette des hôpitaux, 1897; cited by Guelpa: Thèse de Montpellier, 1902. Obs. xii.
29. Delagénière. Arch. Prov. de Chir., 1894; cited by Guelpa: Thèse de Montpellier, 1902. Obs. viii.
30. Delagénière. Arch. Prov. de Chir., 1894; cited by Guelpa: Thèse de Montpellier, 1902. Obs. ix.
31. Ferraresi. Riforma Medica, 1902, xviii, 686. Obs. vii.
32. Gunther. Ueber Atresia Ani, Inaug. Dissert., Bonn, 1902, Fall 9.
33. Hall. Canada Lancet, 1902-3, xxxvi, 543; Pacific Med. Jour., 1903, xlvi, 13.
34. Hutchinson. Records of Children's Hospital, Phila., No. 771 of 1901.
35. Kirmisson. Cited by Guelpa: Thèse de Montpellier, 1902. Obs. xiii.
36. Kirmisson. Cited by Guelpa: Thèse de Montpellier, 1902. Obs. xiv.
37. Laurie. Lancet, 1902, i, 158. Case 1.
38. Montgomery. Lancet, 1900, i, 304. Case 3.
39. Montgomery. Lancet, 1900, i, 304. Case 6.
40. Montgomery. Lancet, 1900, i, 304. Case 7.
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42. Uldall. Hospitalstidende, 1903, No. 31; cited in Centralbl. f. Kinderheilkunde, 1904, ix. 466.
43. Veras. Echo méd. du Nord, Lille, 1906, x, 20.

3. *Atresia Ani et Recti.*

44. John Ashhurst, Jr. Records of Children's Hospital, Phila., July 29, 1879.
45. Chalot. Bull. et mém. de la Soc. de chir. de Paris, 1896; cited by Guelpa: Thèse de Montpellier 1902. Obs. xi.
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48. Günther. Ueber Atresia Ani, Inaug. Dissert., Bonn, 1902, Fall 6.
49. Günther. Ueber Atresia Ani, Inaug. Dissert., Bonn, 1902, Fall 7.
50. Hepburn. British Med. Jour., 1902, i, 1264.
51. Le Conte. Records of Children's Hospital, Phila., No. 521 of 1896.
52. Montgomery. Lancet, 1900, i, 304. Case 1.
53. Montgomery. Lancet, 1900, i, 304. Case 2.
54. Montgomery. Lancet, 1900, i, 304. Case 4.
55. Siter. Records of Children's Hospital, Phila., No. 123 of 1906.
56. Squires. New York Med. Record, 1903, lxiv, 576.
57. Wanous. Jour. Minnesota State Med. Assoc. and Northwestern Lancet, 1906, xxvi, 16.
58. Wharton. Records of Children's Hospital, Phila., No. 399 of 1896.
59. Wharton. Records of Children's Hospital, Phila., No. 942 of 1900.

II. ATRESIA ANI SEU RECTI COMPLICATA CUM COMMUNICATIONIBUS.

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61. Samuel Ashhurst. Records of Children's Hospital, Phila., No. 345 of 1899.
62. Delèpine. Jour. d. Sc. méd. de Lille, 1905, i, 381.
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65. Elgood. Lancet, 1906, i, 1531.
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67. Jayne. Colorado Medicine, 1903–4, i, 89. Case 2.
68. Lacasse. Bull. et mém. de la Soc. anat. de Paris, 1904, lxxix, 66.
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74. Montgomery. Lancet, 1900, i, 304. Case 10.
75. Nolte. Medizink Klini. 1906, ii, 1096.
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77. Trautner. Hospitalstidende, 1904, No. 17; cited in Centralbl. f. Kinderheilk., 1904, ix, 467.

78. Wharton. Records of Children's Hospital, Phila., No. 382 of 1903.

III. ATRESIA ANI SEU RECTI COMPLICATA CUM FISTULIS.

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BOOK REVIEWS.

TEXT-BOOK OF PSYCHIATRY. A PSYCHOLOGICAL STUDY OF INSANITY FOR PRACTITIONERS AND STUDENTS. By DR. E. MENDEL, Professor in the University of Berlin. Authorized Translation. Edited and enlarged by WILLIAM C. KRAUSS, M.D. Philadelphia: F. A. Davis Co., 1907.

This text-book on insanity is entirely different from any other work yet published. In its clearness of expression and thought, it proves the stamp of the teacher. There is no attempt to dilate on controversial questions, but a simple and straightforward systematized statement of the subject of mental diseases, with an explanation and interpretation from a psychological standpoint.

A simple clinical classification is used, which has the merit of preventing confusion in the mind of the student. To this, however, is added Delirium Hallucinatorium as a special sub-heading. Mendel has devoted much time and attention to the elucidation of this clinical type, and it is here stated in a clear and concise manner.

The method of presentation includes a careful study of the general symtomatology and etiology of mental diseases. This embraces about one-half of the book; the second half of the book is devoted to the presentation of different clinical types. In the translation, the author has succeeded in presenting the subject in a simple, readable style and at the same time adhering closely to the German text. This book can be recommended to the student and practitioner in general medicine. It is better adapted, I think, to their needs, than any other exposition of the subject.

D. J. McC.

A TEXT-BOOK OF PATHOLOGY. By ALFRED STENGEL, M.D., Professor of Clinical Medicine, University of Pennsylvania; Physician to the Pennsylvania University and the Philadelphia Hospitals. With 399 illustrations in the text, many of them in colors, and 7 full-page chromolithographic plates. Fifth edition, thoroughly revised. Philadelphia and London: W. B. Saunders Co., 1906.

The newly revised edition of Stengel's *Text-book of Pathology* retains the same general features that have determined its success in the past and have warranted the publication of five editions within the past eight years. The chapters dealing with inflammation, immunity, and parasites have been revised so as to present the latest facts in these rapidly increasing fields of scientific activity. New illustrations have been added and some of the illustrations of former editions have been replaced by others better calculated to picture the condition considered. The success of the book is the best index of its quality. It is not a book intended for the advanced pathologist, but for the student or the practitioner interested in the field of pathology it is of unquestionable value. I think it is the experience of teachers of pathology that the student, at first avoiding as much pathological study as possible, finds his interest readily increasing as soon as he knows sufficient to comprehend the ordinary processes and results of morbid change. By its scope and clearness of presentation of the subject-matter, Stengel's *Pathology* assumes a place high among the books calculated to elevate the plane of medicine in this country by enabling the student to more rapidly acquire the knowledge essential to a comprehension of pathological conditions. R. S. L.

A TEXT-BOOK OF COMPARATIVE GENERAL PATHOLOGY FOR PRACTITIONERS AND STUDENTS OF VETERINARY MEDICINE. By PROFESSOR DR. TH. KITT, of Munich. Authorized Translation by WM. W. CADBURY, M.D., Assistant Demonstrator of Pathology in the University of Pennsylvania. Edited with notes and additional illustrations by ALLEN J. SMITH, M.D., Professor of Pathology in the University of Pennsylvania. Illustrated with 4 colored plates and 131 text illustrations. Chicago: W. T. Keener & Co., 1906.

A Text-book of Comparative General Pathology for Practitioners and Students of Veterinary Medicine is the title of the translation of the well-known German work by Kitt. Though, as the title indicates, it is intended primarily for the use of veterinarians, its value is by no means limited to those working in this field. Most of its chapters deal with general pathological principles applicable to human as well as veterinary medicine. The book will, moreover, be found of assistance to the worker in human pathology by broadening his appreciation of the morbid processes in laboratory animals

used in experimental pathology. It is by no means a book limited to morbid anatomy, but one dealing with the chemistry, physiology, and biology of disease processes as well as the anatomical pictures resulting from the pathological disturbances.

After an introduction, a short, readable chapter is devoted to the history of pathology. A chapter entitled "Disposition Towards Disease" deals especially with the question of immunity. Excepting for the generous and rather confusing use of brackets in this chapter, the general, more substantial features of protection against infections diseases are concisely presented, though naturally, in a field in which each day brings forth so many new facts, some of the newer discoveries in seriology are wanting. Instructive chapters then follow, dealing with such general principles as the inheritance of disease, the course and termination of disease, circulatory disturbances, and the degenerations. The chapter on the process of repair and new formations includes, among other features, the special inflammations, tuberculosis, glanders, actinomycosis, and botryomycosis. The final chapter, dealing with functional disturbances, is naturally of rather more distinctly veterinary significance.

The book is moderately well illustrated. It is regretable that the colored plates, of undoubted foreign production, are so limited in number as to only produce the desire that more of them might have been included. The translation is by W. M. Cadbury, ably edited by Allen J. Smith. The book is practically the only one covering the field it does in German as well as in English, and is one that should prove of great value to students of pathology as well as to students and practitioners of veterinary medicine. R. S. L.

Clinical Diagnosis. A Text-book of Clinical Microscopy and Clinical Chemistry for Medical Students, Laboratory Workers, and Practitioners of Medicine. By Charles Phillips Emerson, A.B., M.D., Resident Physician, The Johns Hopkins Hospital· Associate in Medicine, The Johns Hopkins University. Philadelphia and London: J. B. Lippincott Co.

This book is based, as the author states, on his own experience as physician in charge of the Clinical Laboratory, and Instructor in Medicine, of the Johns Hopkins Hospital and University and upon the clinical records of the ward cases since the foundation of the hospital seventeen years ago.

Frequent and apt reference is made at times to these records, with allusions as to the success with which various methods and tests have been attended; thus giving the work an individuality of its own. The text consists of 627 pages divided as follows: 81 on the sputum, 226 on the urine, 46 on the gastric contents, 38 on the feces, 218 on the blood, and 18 on the examination of various body fluids, devoting to the examination of the sputum a more extended consideration than is usual, discussing its macroscopic appearance in different diseases fully, and giving considerable attention to the value of elastic fibers.

The chapter on the urine is comprehensive and contains a sensible exposition of the possibilities and limitations of urinalysis.

The 46 pages, all that are devoted to the gastric contents, we believe show that Dr. Emerson has a correct estimate of the usefulness to the clinician of examinations of the gastric contents as compared with examinations of the urine or of the blood.

The section treating on the blood is unconsciously enlivened by a delightful account of the Johns Hopkins student endeavoring to be ultrascientific. It reads as follows: "Our students, in studying their own blood have learned to search on the anterior surface of the forearm for the pain points, and, avoiding these, to always prick over a small superficial vein."

Considerable attention is paid to Ehrlich's triple stain; one of the most important of the colored plates shows the blood stained with it; more we think than is advisable, as fewer will use this method each succeeding year, because of the many advantages of the present various Romanofsky modifications and, as also we confidently believe, still better ones will be forthcoming. It is pleasing to see Ehrlich's classification of leukocytes used and the normal cells thus divided into six varieties; until some classification with more weight behind it is advanced, let us adhere to this old classification and be able to comprehend what the differential counts of others really mean. Too often throughout this section are the figures of blood counts or differential counts in one or two cases of many diseases or states of health given, figures that should only be given in averages derived from a number of counts.

The illustrations are almost all original and are finely executed and add much to the book; the colored plates are truly excellent. Perhaps it is the peculiar individuality of the book, of which we spoke earlier, making it different from other treatises on the subject, or perhaps the excessive number of attempts to introduce unimportant asides in the shape of allusions to methods of teaching or efforts to connect the laboratory work with the bedside work, a laudable attempt, but not properly executed; but whatever it is, the book does not appear as well balanced as could be desired.

A great deal of very good material it contains undoubtedly, but in with this there is that which could be removed and leave the work a more attractive one. W. P.

Psychology Applied to Medicine: Introductory Studies. By David M. Wells, M.D., Lecturer on Mental Physiology and Assistant in Ophthalmology, Boston University Medical School, etc. Illustrated. Philadelphia: F. A. Davis Co.

Dr. Wells has handled, in this little book, a difficult subject in a direct and practical manner. The opening chapters on psychology are elementary, but succeed in placing the subject before the reader in a way that admits of its direct application to medical problems. More than half of the book deals in a lucid and fairminded manner with hypnotism, its history, methods of induction, and therapeutic uses and value. C. D. C.

UNIVERSITY OF PENNSYLVANIA

DEPARTMENT OF MEDICINE

FOUNDED IN 1765

This Medical School, the oldest in the United States, was founded in 1765 by Dr. John Morgan, who filled in it the first medical professorship created in America. In his opening "Discourse upon the Institution of Medical Schools in America," delivered in the College of Philadelphia May 30, 1765, Dr. Morgan uttered these prophetic words: "Perhaps this medical institution, the first of its kind in America, though small in its beginning, may receive a constant increase of strength, and annually exert new vigor. It may collect a number of young persons, of more than ordinary abilities, and so improve their knowledge as to spread its reputation to distant parts. By sending these abroad duly qualified, or by exciting an emulation amongst men of parts and literature, it may give birth to other useful institutions of a similar nature, or occasional rise, by its example, to numerous societies of different kinds, calculated to spread the light of knowledge through the whole American continent, wherever inhabited."

Through Dr. Morgan, the pupil of Hunter in London and of Cullen in Edinburgh, the graduates of this school take a just pride in regarding it as the lineal descendant of the best medical schools of Great Britain in the last century. To Dr. Morgan was soon joined another pupil of Cullen, Dr. William Shippen, as Professor of Anatomy and Surgery, thus forming another tie of relationship to the celebrated University of Edinburgh, whose methods of instruction were substantially adopted here. In the next year Dr. Adam Kuhn was added as Professor of Botany and Materia Medica; and in June, 1768, a "Commencement was held," at which medical honors were bestowed, the first in point of time in America. In 1769, Dr. Benjamin Rush was elected Professor of Chemistry, while Dr. Thomas Bond, one of the trustees of the College of Philadelphia, delivered lectures on Clinical Medicine in the Pennsylvania Hospital.

To the faculty thus composed of Morgan, Shippen, Bond, Kuhn, and Rush, have succeeded, at various times, professors whose reputation has been national, such as Wistar, Barton, Physick, Chapman, Hare, Gibson, Horner, Dewees, Jackson, George B. Wood, Hodge, James B. Rogers Carson, R. E. Rogers, Leidy, Henry H. Smith, Pepper, Francis Gurney Smith, Stillé, D. Hayes Agnew, Goodell, W. Pepper, Jr., and Ashhurst.

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Diplomas of public high schools may be accepted as complete or partial certificates. All diplomas presented by candidates will be referred to Faculty Committee No. 1 of the College Faculty (Academic), who will examine each case and decide whether the diplomas shall be accepted in lieu of examinations, and what subjects they properly cover. The diploma must be transmitted to the Dean of the Medical Faculty not later than June 10 or September 10 in each year, and must be accompanied by a certificate signed by the principal of the school, stating the exact amount of each subject covered by the diploma, and the mark or grade attained in each subject.

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THE LEUKOCYTE AND STREPTOCOCCUS CONTENT OF COWS' MILK.

By D. H. Bergey, M.D.,
Assistant Professor of Bacteriology, University of Pennsylvania.

During the course of an investigation upon cows' milk carried out in the summer of 1900,[1] I was forcibly impressed by the fact that when the milk of a cow is rich in leukocytes it also contains, as a rule, considerable numbers of streptococci. I was able to confirm the statement made by Eastes,[2] that whenever pus is found in milk streptococci are also present in much greater numbers than in the milk of healthy cows.

The method which I employed, in this series of investigations, to determine the presence of pus in milk was that which had been employed by Stokes,[3] and I followed his example in regarding an average of five cells in a field of the $\frac{1}{12}$ inch oil immersion lens, in smears prepared from the sediment of 10 c.c. of milk, to indicate the presence of pus. Especially in instances where the cells showed a tendency to form clumps was this number regarded as indicating the presence of pus by Stokes, and my experience led me to adopt the same standard.

During the course of a second investigation along somewhat similar lines carried out in the summer of 1903,[4] the relation of the leukocytic content and the prevalence of streptococci in cows' milk was more definitely brought out. In this second investigation the leukocyte standard was raised to ten per field, as experience had shown that the lower standard was not always safe. The subsequent examination,[5] over a period of about nine months, of several cows encountered during the second investigation, showed that the condition of high cellular content and high streptococcus content is one of inflammation of the udder, and that this disease is frequently confined to one or more quarters of the udder, while remaining portions yield practically normal milk.

The method of determining the cellular content of milk which I employed is crude, and I have always regarded it as being somewhat unsatisfactory, but it proved sufficiently reliable to detect even slight evidences of udder disease, and it was comparatively simple. During the past few years several methods have been devised, some of which are claimed to be far more accurate than the Stokes method. The method of Stewart[6] consists in centrifuging 1 c.c. of milk in a special glass tube, which is closed at each end with a small rubber stopper. The leukocytes lodge on the stopper closing the distal end of the tube. By smearing the sediment on the stopper over a definite area on a clean glass slide, and staining with methylene-blue solution, the number of cells in 1 c.c. of milk is ascertained.

About the same time Doane[7] devised a volumetric method for determining the leukocytic content of milk. 10 c.c. of milk are centrifuged and the cream layer, as well as the milk overlying the sediment, carefully removed. The sediment is now treated with an appropriate stain to color the cells, and the volume of sediment is diluted to 1 c.c. A small portion of the stained sediment is now transferred to the cell of a Thoma-Zeiss blood-counting slide and the number of cells enumerated. Doane claims much greater accuracy for his method than for the Stokes method and in this respect he is supported by a number of later investigators.

Savage[8] devised a method which is almost identical with that used by Doane, except that he employs only 1 c.c. of milk in a 20 c.c. sedimentation tube, filling the tube to the 20 c.c. mark with Toisson fluid, and later removing all except 1 c.c. of fluid.

Slack[9] has modified the Stewart method in that he employs a 2 c.c. tube and spreads the sediment obtained from 2 c.c. of milk over an area of 4 sq. cm. Slack regards the presence of over 50 cells per field of the $\frac{1}{12}$ inch lens as indicating the presence of pus.

More recently Trommsdorff[10] devised a volumetric method which consists in centrifuging 10 c.c. of milk in a specially constructed tube having a graduated point so as to permit the direct measurement of the volume of sediment in the milk. This method does not require any other apparatus than a suitable centrifuge and the specially graduated tubes.

Doane (*loc. cit.*) has reported a number of comparative tests with the Stokes method and with the method which he devised. He considers that the presence of 500,000 cells per cubic centimeter of milk is suspicious, and when the number reaches 1,000,000 per cubic centimeter there is undoubtedly inflammation of the udder. He states that "the Stokes method was so grossly unreliable that any count below fifty per field could not be accepted as showing the milk was suspicious." In Table I of his report he gives comparative estimations of the leukocytes in the milk of nine cows. By the Stokes method each of these cows was giving off pus, while by the Doane method at least three showed pus, while four were suspicious, and the other two showed each about 300,000 cells per cubic centimeter. These tests,

which were evidently made to show the comparative value of the two methods, indicate that the Stokes method is far from being as "grossly unreliable" as Doane would have us believe.

Ward[11] reports a series of comparative estimations of the number of cells in milk as shown by the Stewart and the Doane methods. In averaging his results obtained by the two methods Ward found that in making a series of duplicate determinations by the Stewart method the second series was only 85 per cent. as high as the first series. In the Doane method the second series was 93.2 per cent. as high as the first series. Ward concludes that "the Doane test is far more consistent in every respect than that of Stewart."

Russell and Hoffman[12] also report on a series of comparative tests with the Stewart and the Doane methods. Their results show a far greater degree of variation between the two methods than do those of Ward. While results obtained in duplicate estimations with the Doane method varied only 5.6 per cent., those obtained with the Stewart method varied as much as 112 per cent. They conclude that "from these data it appears, without question, that the volumetric method is very much more accurate for the determination of the actual conditions in milk; and not only in scientific studies on this question, but also in the practical application of any standard in public health work this should be given preference over the smeared-sediment method."

Rullmann and Trommsdorff[13] report on a large series of examinations of milk of individual cows and of mixed milk by the method devised by Trommsdorff (*loc. cit.*). They conclude that when the mixed milk of the four quarters of a cow shows more than 0.1 of 1 per cent., by volume, of sediment, mastitis should be suspected, and when the volume of sediment exceeds 0.2 per cent. disease of the udder is certainly present. Harris,[14] the only American who has called attention to Trommsdorff's method, states that it is open to objection because it gives us only qualitative and not quantitative results such as he claims are given by the methods of Doane and Savage, and moreover the capillary end of the tube may be occluded by foreign material and thus lead to erroneous results.

With regard to the statement which I made in the report of my investigations in 1900 that a high cellular content of the milk of an individual cow was, nearly always, accompanied with a high streptococcus content, and that these conditions indicated the presence of mastitis in one or more quarters of a cow's udder, there has been some variation in the results obtained by different investigators.

Doane (*loc. cit.*) appears to be quite skeptical as to the coincident occurrence of large numbers of cells and of streptococci because in some of the results I obtained very large numbers of cells and encountered very few, if any, streptococci. He seems to lose sight of the fact that the formation of pus under natural conditions always rests upon the presence of certain types of bacteria. In a number of instances I found pus in milk along with large numbers of other bacteria than streptococci. Bacterium pseudodiphtheriticum was found in a number of instances and I believe these organisms are capaple of causing or at least of continuing inflammation when already established.[15]

Savage (*loc. cit.*) states that his results show absolutely no connection between a high cellular content and a high streptococcus content. This statement is apparently due to the fact that, as stated by Savage, practically all milk contains streptococci, and that he has made no attempt to ascertain whether the two bear any numerical relation to each other. Moreover, Savage examined only healthy cows. In one cow where the milk undoubtedly contained pus—10,100 cells per cubic millimeter—he found streptococci in a single loopful of the milk. One of the quarters of the udder of this cow was found to be indurated.

Stewart (*loc. cit.*) condemns market milk when it contains streptococci. Slack[16] condemns market milk when it contains, on microscopic examination of the sediment, streptococci, diplococci, or cocci, and the plate cultures at the same time show colonies resembling streptococci colonies in excess of 100,000 per cubic centimeter of milk, and broth cultures prepared from the milk show streptococci alone or in great excess over the other bacteria present.

Ward (*loc. cit.*) states that "the presence of streptococci in milk cannot be regarded as proof of the existence of active mammitis in the cow." However, there is no evidence in Ward's paper that he sought to ascertain whether a high cellular content of cows' milk had any relation to a high streptococcus content. In view of the fact, now universally conceded, that all cows' milk contains both leukocytes and streptococci, it would be just as fallacious to state that, in consequence, the presence of large numbers of cells did not indicate inflammation, as to state that the mere presence of streptococci, irrespective of their numbers in a particular case, is no evidence that they are the cause of the inflammation, and hence of the high cellular content.

Harris (*loc. cit.*), basing his opinion upon the studies of Heinemann and others with regard to the streptococci found in milk, states that these "cast considerable doubt upon the value heretofore entertained regarding the significance of streptococci in milk." While he concedes their possible relation to mastitis he feels that it is necessary for us to have a "reliable method of distinguishing a non-pathogenic from a pathogenic streptococcus" before we will be in a position to determine their exact significance.

Trommsdorff (*loc. cit.*) states that whenever he found large numbers of leukocytes in a sample of milk he always found large numbers of streptococci also present, frequently in almost pure culture. He examined the mixed milk of each

cow in a stable, and whenever he encountered a cow whose mixed milk showed more than 0.1 of 1 per cent. by volume of sediment he examined, subsequently, the milk from each of the four quarters of the udder. In almost every such instance he found the milk coming from one or more quarters to contain pus and usually also numerous streptococci. He also reports several instances in which he encountered a high cellular content without finding large numbers of streptococci or other bacteria. I have reported several instances of this kind.

Comparative Results Obtained in the Estimation of Leukocytes in Milk.

Number of sample.	Stokes method. Number of leukocytes per field $\frac{1}{12}$ lens.	Stewart method. Number of leukocytes per field $\frac{1}{12}$ lens.	Doane method. Number of leukocytes per c.c. of milk.	Trommsdorff method. Amount of leukocytic sediment in 10c.c. of milk.	Number of bacteria per c.c. of milk. Agar plates 4 days at 20° C.	Presence of streptococci.
1	0.1	25.	32,000	0.1 per m.	6,000	
2	2.0	27.0	33,600	0.1 "	4,050	
3	0.6	25. +	32,000	0.4 "	1,700	
4	0.3	25.	16,000	0.3 "	1,600	
5	0.0	0.6	56,000	0.1 "	1,730	
6	6.0	50. +	640,000	1.1 "	9,140	Present.
7	0.5	19.0	24,500	0.1 "	12,320	
8	2.0	29.5	616,000	0.3 "	18,700	Numerous.
9	25. +	24.3	.....	2.3 "	700	Almost pure culture.
10	25.	50. +	.....	1.1 "	2,240	

I have undertaken a short series of examinations of the milk of individual cows, employing the methods of Stokes, Stewart, Doane, and Trommsdorff, in order to ascertain the relative value of these different methods. The examinations, with the exception of those by the Stewart method, were always carried out in duplicate, so that the results given in the appended table are the means of the several observations made on each sample. The variations in the duplicate tests of a sample were very slight with the Stokes and Doane methods, while those with the Trommsdorff method were usually identical. In two of the samples no estimation could be made by the Doane method, as the cells were massed to such an extent as to preclude counting them.

The Stokes method indicates that at least two of the samples contained pus (9 and 10), and sample No. 10 contained blood also, as indicated by the reddish tinge of the sediment and the presence of erythrocytes in smears stained with Jenner's stain. None of the other samples appeared to be suspicious, except sample No. 6, though there was no distinct evidence of a tendency of the cells to clump in masses. If I were called upon to pass judgment on the ten samples on the basis of the results obtained by the Stokes method I would condemn Nos. 9 and 10 as containing pus.

[1] These samples of milk were not collected in sterilized containers, hence many of the bacteria in some of the samples did not come from the cows' udder.

Stewart regards the presence of twenty-two cells per field of the $\frac{1}{12}$ inch lens as indicating pus, and judged on this basis all except two of the samples would have to be condemned. In many of the samples the cells were so massed together that an accurate enumeration could not be made.

The results obtained by the Doane method indicate that samples 8, 9, and 10 contain pus, while sample No. 6 is highly suspicious. Sample No. 6 was also suspicious according to the Stokes method, and would have been condemned under the Stewart method. This sample contained also 0.11 of 1 per cent., by volume, of sediment in the Trommsdorff test. Sample No. 8 would have been condemned also according to the Stewart method, but the only other objectionable feature is the fact that the plate cultures showed the presence of numerous streptococci.

The only samples that would be condemned according to the Trommsdorff method are samples 6, 9, and 10, which are also condemned by all the other methods, and besides they contained almost pure cultures of streptococci.

The results obtained by these different methods indicate that the Stokes method is not so grossly unreliable as some investigators claim, and neither are the Stewart and Doane methods as trustworthy as could be desired. The few tests here recorded indicate that the method devised by Trommsdorff is more reliable than any yet proposed, from the fact that it is possible to obtain exactly the same results in duplicate tests on the same milk, which cannot be done by any of the other methods, however well trained the person may be. In the hands of unskilled persons the results obtained by the Doane method would be absolutely useless, while no great skill is required to employ the Trommsdorff method.

The only criticism of the Trommsdorff method raised by Harris, that may influence the results, is the presence of dirt in the milk. This objection would not hold in milk that is collected and marketed in the proper way, and would not hold where the investigator collects the milk in stables from individual cows.

In all my reports I have emphasized the fact that practically all milk contains both leukocytes and streptococci, and it is only when these constituents are present in large numbers do they have a pathological significance. There is abundant evidence at hand to support the statement that they bear the relation of cause and effect, and that the presence of large numbers of pus cells and of streptococci in the milk of a particular cow are positive evidence of the presence of inflammatory trouble in the udder.

The degree of mastitis existing in particular cases may be so slight as to make the detection of induration, by a competent veterinarian, most difficult. In like manner many human beings suffer for years from slight catarrhal conditions of the mucous membranes of the upper respiratory tract, yet external conditions and general health of the individual

give no indication of the diseased state of these tissues. In a similar way an actively secreting gland like a cow's udder, with its abundant blood supply, is most probably subject to similar disturbances.

The statement that "the sanitary significance of the so-called 'pus cell' has been greatly overrated" is one that cannot be allowed to go unchallenged. If for no other reason than a purely esthetic one it would be undesirable to permit the sale of milk containing pus. When we know that in addition to the pus such milk usually contains streptococci the sanitary significance becomes evident. Not a few authentic instances are on record where the use of milk of this character has proved injurious to those using it. Moreover, it is quite probable that some of the grave forms of infantile diarrhea are directly due to infection by streptococci derived from cows suffering from mastitis.

Cows' milk undoubtedly contains several varieties of streptococci, but the variety which is concerned in the normal souring of milk can be differentiated from the pyogenic variety found in the cases of mastitis. Whether the variety of streptococcus concerned in the souring of milk (the so-called Bacterium lactis acidi) has any sanitary significance cannot be stated at this time.

The following conclusions may be drawn from the work on the subject of the relation of leukocytes and streptococci to cows' milk:

1. Of the different methods proposed for determining the presence of pus in cows' milk that of Trommsdorff is the simplest and at the same time yields the most reliable and concordant results.

2. Practically all milk contains some leukocytes and streptococci. Only when these constituents are increased to a certain extent are they indicative of pathological conditions in the udder.

3. In practically all cases where the number of leukocytes is high there will also be found a relative increase in the number of streptococci, indicating the presence of mastitis in one or more quarters of the udder.

4. Careful palpation of the empty udder, by a competent veterinarian, usually reveals the presence of an indurated area in the infected quarter of the udder.

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REGENERATION OF BONE.

An Essay, Illustrated by Photographs and Photomicrographs, Dealing with the Repair of Simple Fractures and the Regeneration of Bone after Partial Injury and Subperiosteal Resection.

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INTRODUCTION.

The subject of regeneration of bone, especially with reference to the repair of fractures, has occupied the attention of scientific writers from the earliest days of medical history to the present time. Research along this line was especially active in the latter part of the eighteenth and the early part of the nineteenth century. It was revived by the work of the naturalist Duhamel du Monceau, who called attention to the active part played by the periosteum in the repair of bone and later by the enduring work of the great French surgeon, Dupuytren, who placed the subject upon a scientific basis. In spite of the tremendous amount of labor that has been devoted to the investigation of this subject, there

has never been even a fair amount of unity of the opinions of the writers upon the subject. As far as I am able to judge, about the only subject on which everyone agrees is the fact that the bone unites. As to which portion or portions of the bone are responsible for that union there are almost as many opinions as there are writings, so that one is left in a maze when he endeavors to arrive at conclusions by reading the literature.

Being cognizant of the above and at the request of Dr. Frazier, the writer was induced to take up the subject in order to endeavor to formulate an opinion that would be satisfactory to himself and to try to clear up some of the haze that surrounds the subject. In almost all writings upon this matter, the authors have begun by giving a chronological account of the work done by others and then proceeding to combat the facts contained in these writings. In view of the fact that there are already so many sources from which to obtain this knowledge, and since this paper is nowise based upon work done by any writer, with the possible exception of Dupuytren and Nichols, it is deemed unnecessary to lengthen the article by repetition, but it is proposed to let the paper itself present the writer's findings and deductions. Very little reading upon the subject had been done previous to the completion of the work and the formulation of opinions, so that the writer should not be biased in his views, thereby working according to preformed ideas. Due attention will be given to the work of others in the portion of the paper devoted to conclusions, where the opinions of the most important writers will be compared with the views contained in the paper.

Before proceeding with the body of the paper, I wish to express my gratitude to the authorities of the University of Pennsylvania, especially Dr. Chas. H. Frazier, for the privilege of conducting the experiments in their laboratories and for the abundant facilities and material they placed at my disposal. I also take this opportunity to thank all who have by their advice, encouragement, or assistance aided me in bringing this study to a successful conclusion.

SYNOPSIS OF EXPERIMENTS.

The work of experimentation has covered a period of two years, during which time about 135 experiments have been performed upon rabbits and dogs. This number has been decreased considerably by loss through infection (very great in the beginning, due to poor facilities which were improved later), and owing to the fact that some of the animals and gross specimens were lost. No experiment has been included in which there was non-union of a well-recognized degree. In addition, about fourteen rabbit experiments were used in developing the proper technique for grinding the specimens. As a result of the losses from various sources, this paper is based on the reports of sixty-four dog and seventeen rabbit experiments.

The experiments have been divided into fifteen series, each for the purpose of determining the individual activities of certain portions of the bone independent of other factors. The different series, with their purposes, were as follows:

Series 1. Upon rabbits, to study complete fractures from the first day until about the thirty-fifth day, to determine the action of all the tissues from the earliest period until the full development of the callus. The technique was carried out in such a manner (see Technique) that none of the soft tissues were removed, but the region of the fracture studied in its entirety.

Series 2. Upon dogs, to study the later developments in the callus during the process of union. The experiments consisted in making complete fractures of the tibia.

Series 3. Upon dogs, to study the result of injury to all portions of the bone, independent of extrinsic forces. In this series, an effort was made to cause a complete fracture of one-half of the bone, leaving the other half intact in order to maintain perfect position and prevent any mobility of the ends of the fragments.

Series 4. Upon dogs, to determine the activity of the medulla and cortex independent of the periosteum. It was a repetition of the last series with the exception that the periosteum was removed in the region of the fracture.

Series 5. Upon dogs, to determine the activity of the cortex independent of the periosteum and the medulla. The experiments consisted in removing the periosteum and making superficial injuries to the bone without entering the medullary cavity.

Series 6. Upon dogs, to study the activity of the periosteum raised from the bone, when accompanied by injury to the bone not sufficiently deep to enter the medullary cavity.

Series 7. Upon dogs, to determine whether an animal substance placed under the periosteum, when not accompanied by injury to the bone, would cause the formation of osseous tissue. Catgut was the substance used.

Series 8. Upon dogs, to determine whether an unabsorbable foreign material, placed under the periosteum, without additional injury to the bone, would excite the formation of new osseous tissue. In this instance celloidin hardened in bichloride alcohol was used.

Series 9. Upon dogs, to determine the influence, upon osteogenesis, of blood clot under the raised periosteum, when not accompanied by injury to the bone.

Series 10. Upon dogs, to determine the effect of merely raising the periosteum, with as perfect hemostasis as possible and without injury to the bone.

The next four series were performed with the object of determining the possibility of regeneration of the tibia after

Nichols' subperiosteal resection, when not in the presence of inflammation. They were as follows:

Series 11. Upon dogs, to determine the influence upon regeneration exerted by allowing a small bridge of osseous tissue to remain under the periosteum, instead of removing the entire section of bone.

Series 12. Upon dogs, to determine the activity of the periosteum alone. These operations consisted in typical subperiosteal resections.

Series 13. Upon dogs, to determine the influence exerted upon regeneration by the periosteum, when the medulla is replaced between its layers after the removal of the cortex.

Series 14. Upon dogs, to determine the influence upon regeneration exerted by bone salts deposited between the layers of the periosteum, after the removal of the cortex.

Series 15. Upon rabbits, to determine, if possible, what role the fibrin took in the formation of cartilage. The experiments consisted in making complete fractures and, at very short intervals afterward, exposing the area injured and making smears and sections from the callus. Unfortunately the results of this series are negative, owing to defective technique.

TECHNIQUE.

In the first, or rabbit series, in which complete fractures were made without incision of the skin, an effort was made to maintain the relations just as they were at the time of death without removing the tissues surrounding the site of fracture. To accomplish this two methods were employed: First, the entire leg, denuded of skin, was placed on the stage of a freezing microtome and frozen hard. The entire leg was then cut through at a fair distance from the site of fracture and the tissues placed in Müller formol for several days, to harden before decalcification. Later it was found that freezing was not necessary, so, in its stead, the specimens were immediately placed in Müller formol and after a day or two they were found hard enough to cut across in the manner described in the freezing method. This method was used with the later specimens. After cutting the specimens and leaving them in Müller formol for another day or two to harden further, they were washed for twenty-four hours in running water and then placed in the decalcifying fluid.

The decalcifying fluid which was used for the rabbit experiments and the earlier dog experiments consisted of nitric acid 5 per cent., about 1 per cent. formalin, 5 per cent. of a saturated aqueous solution of picric acid, and water to make 100 per cent. This fluid was not as good as the one which will be given later under the technique of the dog experiments, as it does not give good nuclear staining

The specimens were decalcified until they could be penetrated with a pin and were then washed for several days in running water, 95 per cent. alcohol for several days, absolute alcohol for twenty-four hours, absolute alcohol and ether for twenty-four hours, and three strengths of celloidin. After three weeks' embedding in celloidin they were mounted and cut on a Minot precision microtome. These specimens were not as good as they might have been had the fluid used in the later dog experiments been used, and had they been washed in alcohol until all yellow tint had disappeared from the wash alcohol after standing twenty-four hours. This is a very important step, as the water is not so effectual in removing the picric acid as is the alcohol, and unless every trace of it is removed the picric acid interferes with the embedding and, very materially, with the staining, the tissues either refusing to take the stain or losing it very promptly afterward. The acid also acts on the celloidin so that it refuses to harden in the mounting of the specimens. The embedding of the deeper portions of the specimens might have been better had the dense outer layer of deep fascia been removed so that the celloidin could more easily penetrate the tissues

The technique in the dog experiments differed somewhat, owing partly to the fact that the specimens had to be divided to be embedded in two different manners, and partly as the result of the recognition of the defects in the process as originally carried out. The animals were killed with chloroform or gas and the legs were immediately amputated and prepared for fixing. The conditions of the wound were noted and then the skin carefully removed so as not to interfere with the operated area of the bone. Muscular tissues were removed and a section of the bone retained, which went wide of the site of the operation in order to include all possible callus or changes in the bone as the result of injury. This section was immediately placed in 50 per cent. formalin, although 20 per cent. formalin was used on several occasions without apparent difference in the results. In three or four days, depending on the size of the section, it was removed from the formalin, washed in water for a time, placed in a vise and sectioned longitudinally with a specially devised saw, bisecting the operated area and the medullary cavity. This was done so that a section could be run through the celloidin embedding, and another section run through the balsam embedding for grinding. A description of the macroscopic appearances was noted and the two sections again placed in 4 per cent. formalin to fix whatever portions of the medulla may have escaped fixation in the several previous days. After several days of rehardening the specimens were washed in water for twenty-four hours and then one-half was run through celloidin and the other half through balsam embedding.

The saw mentioned above was on the principle of the

jeweller's saw, only a little firmer and about five-eighths inch wide to maintain a straight direction as it went through the bone. Alternate teeth were deviated to one side or the other to prevent jamming of the saw in the deeper portions of the cut.

The specimens to be cut in celloidin were immediately placed in the decalcifying fluid, which originally was that used in the rabbit experiments. Later it was found that the efficacy of the fluid could be greatly enhanced by the addition of 15 per cent. alcohol (95 per cent.). When this fluid is used, very good nuclear staining can frequently be obtained. When the specimen was penetrable with a pin it was washed in running water for two or three days, followed by alcohol, which was changed daily until there was not the slightest tint of yellow in the alcohol on standing twenty-four hours. The specimen was then run through absolute alcohol, absolute alcohol and ether, and, after being in two or three thicknesses of celloidin for three weeks, was mounted and cut. The thickness of the cut sections varied greatly. All were stained with hematoxylin and eosin.

Balsam Embedding. In order to see what could be learned from specimens ground to microscopic thinness without previous decalcification, one-half of each bone was run through a process of embedding after the style of Weil's process, but with modifications, the result of previous experimentation. The specimens were hardened in formalin in the manner described, washed in water, and then again hardened in 95 per cent. alcohol for a few more days. Following this they were rinsed off in water and placed in Grenacher's borax-carmine stain. They were left in this solution eight days, as it is very slow-acting, and specimens cannot be overstained with it. After this the sections were placed immediately in acid alcohol (1 per cent. hydrochloric acid in 70 per cent. alcohol) without preliminary washing in water.

They were allowed to stay in this solution for about forty-eight hours, then transferred to 95 per cent. alcohol for twenty-four hours, absolute alcohol twenty-four hours, cedar oil twenty-four to forty-eight hours, xylol for a few minutes, and then a thin solution of xylol balsam. This xylol balsam is not the usual balsam used in mounting specimens on slides, but is made by first evaporating paper-filtered Canada balsam to dryness, to rid it of turpentine, and then adding this hardened balsam to xylol.

The best dish in which to evaporate balsam has been found to be a sheet-steel sand-bath. This will not rust readily, is more or less pliable, and, in addition, does not break in the effort to remove the balsam. If a porcelain dish is used the balsam must be dug out with a sharp knife or instrument, and the chances are strongly in favor of penetrating the bottom of the dish. With the sheet-steel one, by tapping the bottom of the dish and bending in the sides, the balsam can be removed as a single large mass and later broken into fine pieces.

The specimens were allowed to remain in thin balsam for a few days and then each day a little powdered balsam added until, at the end of a week or so, the xylol was saturated with it. In a couple of days the specimens were ready for evaporating. This was done by placing them in shallow watch-crystals, with the important area downward, covering the specimens partially with saturated xylol balsam. The watch-crystals were placed on a sand- or water-bath for evaporation. This is a very slow and tedious process, as the water should not go above 95° C., for otherwise the specimens will be cooked. Where there are facilities for constant observation, and where there are not many specimens to be evaporated, the water-bath is the better of the two, as the temperature can be more easily regulated and the specimens be evaporated more quickly. The sand has a tendency to get too hot or too cold, and is rather hard to regulate. Even when the temperature of the sand is higher than the water it does not appear to do the work so well. The sections were identified by labelling the crystals before pouring on the balsam. The balsam protects the labels and the writing is visible through the transparent mass.

When the specimens had become so hard that the balsam, when cooled, fractured on the insertion of a sharp instrument, they were ready for grinding. The balsam had to be brittle, for otherwise the grinding on the rapidly moving disk would have heated it and made it drag, not grinding off clean and sharp. The specimens were readily removed from the crystals by melting a thin layer of balsam on the bottom by passing it through a Bunsen flame. This allowed the entire mass to be pushed off and rapidly cooled under running water to cool the mass before the balsam around the specimens also became soft.

The machine used in grinding the specimens was a modification of the machine devised by Dr. Frederick Allen, of the Dental Department of the University of Pennsylvania. The modifications are unimportant, being merely the addition of another drip spigot on the opposite side, so that the grinding surface should never become dry, and the widening of the drip pan to save rusting of the machine. An accurate description of the machine can be had by referring to the original article of Dr. Allen. The idea of the machine is to afford a means of controlling, with comparative accuracy, the thickness of the specimens to be ground by means of mathematically accurate screws, etc., to control the platens and grinding disks. It is a vertical lathe of very fine adjustment. Mr. Cowarden, of Richmond, Virginia, has ground some very fine sections of bone with the soft parts detached by means of a horizontal lathe of cruder construction.

The grit that gave the greatest satisfaction was finely

powdered glass. Pumice and carborundum were tried, but both leave the specimens, especially the soft tissues, in an extremely dirty condition. By means of a very thin suspension of powdered glass, sections have been obtained which are practically free from dirt. I believe that this result has not been obtained hitherto by other means.

The specimen to be ground was held by the fingers against the rapidly moving disk, upon which a watery suspension of powdered glass was placed with a brush, until a flat surface was obtained and the specimen reached. It was then ready to be placed on the platen. This was done by means of balsam that had been hardened until it would fracture on the introduction of a pin, but not so hard and brittle as the balsam around the specimen, for if this balsam were made too brittle it would lose some of its toughness and the specimen would readily come off the platen during the process of grinding. A thin layer of balsam in the liquid state was obtained by heating the platen with powdered balsam upon it. The specimen was placed firmly on it and rapidly chilled by placing it under running cold water. The platen was then placed in the machine and the disk run with the powdered glass on it until the specimen was ground down to the particular area desired for study, when no more glass was added, but the disk kept running with a liberal supply of water on it to wash out whatever glass had been caught in the meshes of the bone.

The one side was then completed, but the section may still have been very thick or the side that had been ground by hand not very even. Therefore, it had to be transferred to another platen to grind the other side. Before this was done the zero point for the platen to be used was determined on the machine. Zero is the point at which, when swinging the arm of the upright platen holder, the platen will just barely escape the grinding disk. When this was determined, an indicator was screwed into place at the zero point on the screw index.

The platen was then removed, covered with a thin layer of melted evaporated balsam, the ground surface of the specimen on the original platen forced into this film so that the rims of the two platens coincided, and the whole thing placed under running cold water. This left the two platens united by the section between. To remove the first platen it was held in the flame, the heat of the metal soon melting a thin film of balsam on its surface without affecting the section. It could now be easily removed, leaving the specimen on the second platen. After again cooling it was ready for final grinding.

The grinding was done rapidly until about thirty points from zero was reached, when caution was observed and the specimen frequently inspected to determine its thickness. The machine was supposed to give the exact thickness, but the varying thickness of the layer of balsam beneath and of the amount of grit placed on the machine made the eye a better judge of the thickness than the screws. I have lost a number of beautiful specimens by giving the screw just another turn and finding my section ground to nothing.

When the specimen was as thin as desired and had been washed by allowing the machine to go with nothing but water upon the disk, it was ready to be removed and mounted. This was done by moistening it with gasoline upon a towel and then pouring thin celloidin over it. This was either hardened in alcohol or allowed to harden in the air. The platen was then immersed in benzole until the specimens dropped off, to be followed by another change of benzol to remove the excess of balsam that might still remain, carbol-xylol to clear the celloidin, xylol, placed on a slide and covered with xylol balsam and cover-slip.

The illustrations are, for the most part, photographs of the original specimens. All the microscopic pictures, with the exception of one, are photomicrographs of the specimens themselves taken by Mr. Louis Schmidt. This one and one gross picture are black and white wash drawings made by him. The radiographs are positives made from negatives of the specimens with all the soft parts attached. They were made by Dr. Pancoast, of the University Hospital. The radiograph of the human ulna was made by Dr. Newcomet, of the Presbyterian Hospital.

COLLECTIVE REVIEW OF INDIVIDUAL SERIES.

SERIES 1.

In this series the rabbits were placed under the influence of an anesthetic, usually ether (with the occasional use of chloroform), the foreleg grasped between the fingers and broken. The legs were then wrapped in cotton and a sodium silicate bandage applied. It was extremely difficult to keep the dressing on the animals, it being frequently necessary to reapply them several times. Grossly, from the third to the eighth day, there was no union of the fragments, but the mobility did not appear to be as great as when the leg was first fractured. Apparently, there seemed to be something gluing the fragments together without giving the impression of distinct union. On the ninth day there was an absence of lateral mobility, but there was some rocking of the fractures distant from the site of the fracture. From the twelfth to the eighteenth day there was fair union of the fragments, and from that time on the union was good.

Microscopically, most of the specimens, with the exception of the greenstick fractures, show considerable fragmentation of the ends of the bone and displacement of the fragments. Even from the first day the specimens present a remarkably small amount of free corpuscular blood and none was noticed after three and a half days. There was only a very moderate

leukocytic infiltration noticed, and none at all after three and a half days. The feature to which especial attention should be called, and concerning which I have seen practically no mention, is the abundance of fibrin in the region of the fracture. This is present on the first day as a loose network. By the second day it begins to form dense masses, in addition to finer networks containing corpuscular blood in its meshes. By the fourth day it is present as compact masses or streams coursing between the ends of the fragments (Fig. 1). It continues to be present in the form of masses until about the sixth day, when it disappears gradually until about the tenth day, although vestiges of it were found as late as the fourteenth day.

As early as the second day the periosteum and endosteum exhibit signs of proliferation. The cells of the periosteum multiply, with the formation of three or four layers of spindle cells having oval, vesicular nuclei. A formation of a similar

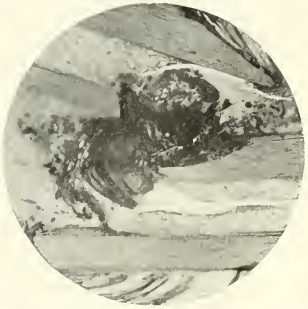

Fig. 1.—Experiment 5, Series 1, fracture four days. Shows lateral displacement of the fragments and dense "streams" of fibrin coursing between their ends.

layer of cells distant from the site of the fracture occurs also in the endosteum, with the exception that some of the cells are slightly more polygonal in shape. The blood appears to have lacerated the medulla farther up on the side of the bone than in the centre. The medullary tissue shows an increase of connective tissue between the fat cells, with a commensurate decrease in the number of these cells. The muscular tissue is infiltrated with blood and a fine network of fibrin. It is beginning to show evidences of connective-tissue hyperplasia, young fibroblasts being present between the fasciculi here and there throughout the muscular tissue.

This process continues for the next two days without any marked changes taking place. On the fourth day differentiation occurs in the periosteum and endosteum at some distance from the site of fracture. The periosteum exhibits considerable hyperplasia of both its superficial fibrous layer and its deeper osteogenetic layer, with the formation of large polygonal cells having large vesicular nuclei. At some distance from the site of fracture the cells appear to fuse, or the ground substance between the cells to become more hyaline and transparent, the whole taking on a homogeneous red stain with eosin, in the form of lines running vertical to the surface of the cortex. These bridge over to meet each other a short distance from the cortex (Fig. 2). Some of the cells are included in the mass and nothing but their nuclei is apparent. Further experiments demonstrate that this is only apparent, since a small amount of protoplasm is included with the nucleus, but greatly compressed by its confined quarters. The above is the first evidence of osteoid tissue in the periosteum, and particular attention is called to the fact that this transformation occurs at some distance

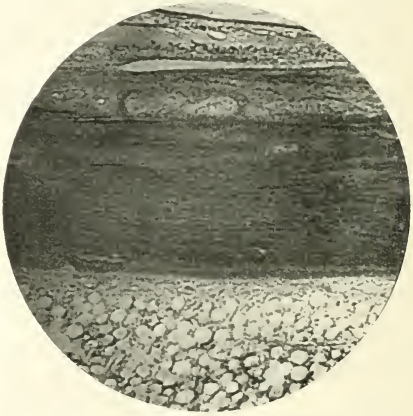

Fig. 2.—Experiment 5, Series 1, fracture four days. Illustrates the earliest formation of trabeculæ in the periosteum. The picture includes one side of the cortex with the periosteum above and the medulla below. The new trabeculæ are seen to bridge over to meet each other.

from the line of fracture. Nearer to the ends of the fragments the cells of the periosteum appear to be embedded in a more or less homogeneous groundwork which does not take the eosin staining and which is without definite arrangements of the cells, the whole having more the appearance of forming cartilage than of anything else. Attention is called to the fact that this occurs nearer the masses of fibrin than does the osteoid tissue.

While the above is taking place in the periosteum, a similar process is occurring in the medullary cavity. The endosteum is also showing proliferation, with the formation of the same large polygonal cells having a small amount of transparent substance between the cells. This substance apparently increases, as in the periosteum, and fuses with the

protoplasm of the cells, the whole again assuming a homogeneous red staining, in lines, with the formation of the trabeculæ. These project from the inner side of the cortex in a manner similar to the periosteal trabeculæ on the outside. This process, also, occurs at some distance from the site of fracture. In the medulla there is a continual increase in the connective-tissue hyperplasia between the fat cells. The muscular tissue exhibits an increased amount of young connective tissue between the fasciculi.

After the fourth day there is always abundant osteoid tissue on the periosteal aspect and also considerable amount in the medullary cavity, though less than in the periosteum. It continues increasing in the periosteum until the ninth day, when osteoclasts make their appearance in the form of large polynuclear cells, which apply themselves to the sides of the trabeculæ. These, by some chemical or phagocytic action, dissolve out the lime salts and destroy the trabeculæ. Their mode of action will be taken up later. These cells, from the ninth day on, continue to absorb the newly formed trabeculæ, while new deposits by osteoblasts are occurring in other places. Their early appearance is probably with the purpose of forming new channels or spaces more in conformity with the line of the bone. The medullary trabeculæ have undergone but little absorption in any of the specimens. From the twelfth day there is absorption of the cortex, increasing commensurately with the duration of the fracture.

The line of fracture and the deposit of cartilage will next be considered.

As stated before, until the tenth day the material between the fragments consists mostly of fibrin and detritus, with fragments of bone, etc. From the fourth day onward, on the periosteal side of the fracture, there can be noted varying amounts of cartilage. Some of it is hyaline in character with very large cells, having even, in a few cases, a twin arrangement. Other specimens contain fibrocartilage. In some areas there appears to be almost a transition from fibrin into cartilage through invasion by connective tissue, with the conversion of these connective-tissue cells into cartilage. The appearances are not conclusive, but suggestive. On the outskirts of the cartilage are seen distinct areas of transition into osteoid tissue, the ground substance increasing in amount and assuming a red color while the cells shrink. This occurs in certain streaks, leaving, in areas, solid islands of cartilage between. In other locations these islands, or at least the ground substance of them, appear to have been absorbed with the liberation of cells, accompanied by penetration of bloodvessels and connective tissue, forming marrow cavities between the trabeculæ. By reference to chart No. 1, it can be seen that the cartilage appears between the ends of the fragments as the fibrin disappears, one specimen showing the two existing together across the line of fracture. The close proximity of the cartilage to the small amount of fibrin that is still remaining between the ends of the fragments is well illustrated by Fig. 3, from a fracture of eight days' duration, which was merely greenstick.

The fact that cartilage is not a growth from the periosteum alone is demonstrated very clearly by the same figure. In this instance some of it is to be seen in the medullary cavity. It could hardly be from a shred of periosteum left in the medullary cavity, for the fracture was so slight that there was not sufficient displacement to allow a shred of periosteum to become detached and left there.

Fig. 3. Experiment 9, Series 1, fracture eight days, greenstick. Demonstrates the close proximity of the remnant of fibrin between the fragments to the small masses of cartilage on the periosteal (above) and medullary aspect of the cortex.

Thus we find that the tissue, holding together the fragments and spindles of osteoid tissue, giving the impression that the fracture is entirely healed, is cartilage and not bone at all, for in none of the experiments up to thirty-five days are there any osteoid trabeculæ to be found between the ends of the fractured cortex.

The typical appearance of a fracture which has been maintained in good position and in which there has been nothing to interfere with union is seen in Fig. 4. It shows well the internal and the external splinting of the sides of the cortex with periosteal and medullary trabeculæ; shows the hyperplastic condition of the marrow, which is continuous in a narrow channel between the two spindles of medullary callus; and shows that between the fragments themselves there is connective tissue and cartilage, but no osteoid tissue. This figure also well illustrates the osteo-

porosis that occurs in the ends of the fragments forming communications between the intertrabecular medullary spaces and the old Haversian canals.

The amount of displacement and mobility of fragments determines, to a great extent, the size of the callus and the rapidity of final union. This fact is demonstrated by a greenstick fracture in which there had been, probably, very little displacement, and in which in the course of twenty-one days had proceeded to almost complete union. It shows well the external splint of dense osteoid trabeculæ in which there is absorption of the deeper portions and also illustrates the absorption of the cortex. There do not appear to be many osteoid trabeculæ remaining in the medullary cavity. Osteoclasts are present in abundance. Between the ends of the cortex there still remains connective tissue and not bone, showing that the process is not as yet complete.

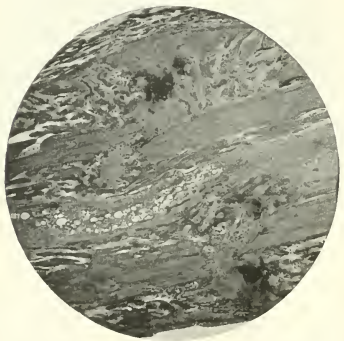

Fig. 4.—Experiment 12, Series 1, fracture twelve days. Illustrates the endosteal and periosteal splints that maintain the position of the fragments. There are small islands of cartilage in the periosteal splints at the line of fracture, but there is only fibrous tissue between the ends of the fragments.

Before concluding this series there remain some isolated facts to be stated. In the first place, in some of the fractures which appear to be fairly well united, the ends of the bone do not seem to exhibit union with any character of tissue, but appear to lie loose in the tissue between the fragments and to be held in place merely by the external cartilage splints. In the red hypertrophic marrow of the bone there are numerous large cells with a large amount of protoplasm, and very large nuclei which show a tendency to divide in some cases. These cells are probably the osteoclasts in the process of formation or in a state of inactivity. Finally, there is little tendency to absorption on the part of the detached fragments but more frequently there is a deposit of osteoid tissue on the surface. Eighteen successful rabbit fractures were obtained in this series.

SERIES 2.

For the sake of making investigation complete and of studying the later changes that occur in the callus (in the line of Dupuytren's idea) Series 2 was performed. Dogs were used because of their more robust nature and because of the fact that they can be more easily dressed and the relations of the fragments better maintained. In each case the animal was etherized, the foreleg grasped firmly between the two hands and fractured over the side of the table. The fracture was then reduced and a shaped wooden splint applied, after a liberal application of cotton, the splint being held in place by a sodium silicate bandage. The animals were killed at periods varying from twenty-one to two hundred and seventy-seven days, the latter being the longest time in the experiments. Nine legs were broken in this series.

Examination of Chart 1 (of the rabbit series) and Chart 2 (Series 2) demonstrates how closely the condition of the repair in the two classes of animals coincide. Almost the same result has been obtained in the rabbit of eighteen days and the dog of twenty-one days, with the exception that the dog leg is not so firm, there being more weight to be carried, the animal being of a larger species. In both, osteoid trabeculæ are present in the periosteum and in the medullary cavity, but none between the fragments. In both, there is absorption of the periosteal trabeculæ and cortex, with questionable, if any, absorption of the medullary trabeculæ. Both show hyperplasia of the marrow and cartilage in the periosteum, with cartilage and connective tissue across the entire line of fractures. With this close relationship between similar fractures in the two species, the series can be considered continuous and the results in one species applied to the other. The dog experiment even shows a small remnant of fibrin on the outskirts of the cartilage and connective tissue separating it from the bone. All the fractures of this series appear, clinically, to be firmly united, excepting two in which there was slight rocking mobility.

Until we reach fractures of very long standing, cartilage in the periosteal callus was found to be present constantly. The amount of this callus and its shape was found to be dependent on the amount of lateral and especially angular displacement. In the fractures of twenty-one and thirty-five days (Fig. 5), there was no angular displacement, so that the cartilage was present merely as a line on the periosteal aspect of the line of fracture. Later on in the series, where angular displacement of the fragments during the process of union did occur, the cartilage took a definite shape, namely, wedge or bracket shape, with the point toward

the space between the ends of the cortex of the fractured bone and the base outward against the periosteum. The width of this bracket was in direct proportion to the amount of angular displacement of the fragments. The amount of periosteal callus on the internal side of the angle was also increased in direct proportion to the amount of displacement. It was proportionately decreased on the opposite side, in some instances being very small in amount (Figs. 6 and 7). Sufficient osteoid tissue is formed on the internal aspect of the angle to again reëstablish the general line of the bone from one point to the other in order to stand the strain required to perform the function of the limb. The denser portions of the new trabeculæ are on the most external portions of the callus, extending as a solid line from the old cortex to the base of the wedge of cartilage. In the deeper portions the callus is much more cancellous in appearance. Microscopically, this is seen to be caused by great osteoclastic absorption of the deeper layers of the trabeculæ in lines

Chart 1.

Number.	Series.	Days.	Free blood between fragments.	Leukocytes.	Fibrin between fragments.	Trabeculæ in			Absorption of			Connective-tissue hyperplasia of medulla.	Cartilage in			Changes in muscles.	Apparent union.
						Periosteum.	Between fragments.	Medullary cavity.	Periosteal trabeculæ.	Medullary trabeculæ.	Cortex.		Periosteum.	Between fragments.	Medulla.		
1	1	1	Lit.	Mod.	Loose Netw.	—	—	—	A	A	—	—	—	—	—	Fragmentation.	—
2	1	2	—	Few.	Mass.	—	—	—	A	A	—	+	—	—	—	Free blood, fibrin.	Greenstick (?).
Greenstick.																	
3	1	3	Lit.	—	Mass. Netw.	—	—	—	A	A	—	+	—	—	—	Fibroblasts.	Very slight.
4	1	3½	Lit.	Few.	Mass. Netw.	—	—	—	A	A	—	?	—	—	—	Fragmentation, blood.	?
5	1	4	—	—	Mass.	B	—	+	—	—	—	+	+ ?	—	—	Conn. tiss.	—
6	1	5	—	—	—	+	—	+	—	—	—	+	+	+	—	Conn. tiss.	Slight.
7	1	6	—	—	Mass.	+	—	— ?	?	?	+	+	+	—	—	?	Slight.
8	1	7	—	—	+	+	A	+	—	—	—	+	—	—	—	—	
Bone forceps.																	
9	1	8	—	—	Lit.	+	—	+	—	—	Lit.	+	+	—	+	—	Greenstick.
10	1	9	—	—	Lit.	+	—	+	+	—	—	+	+	—	—	Conn. tiss.	Rocking.
11	1	10	+	—	+	+	A	+	—	—	—	+	+	—	—	—	
Bone forceps.																	
12	1	12	—	—	—	+	—	+	+	+	+	+	+	Lit.	+	—	+
13	1	13	—	—	—	+	—	+	+	—	+	+	+	+	—	?	—
14	1	14	—	—	+	+	—	+	+	—	+	+	+	+	—	Conn. tiss.	Fair.
15	1	18	—	—	—	+	—	+	+	—	+	+	+	+	+	Conn. tiss.	+
16	1	21	—	—	—	+	—	+	+	+	+	+	—			?	+ greenstick.
17	1	24	—	—	—	+	—	?	+	..	+	..	..	+	..	.....	+
18	1	35	—	—	—	+	—	Lit.	—	—	—	+	+	+	—	Conn. tissue.	+

Explanation: + present. — absent. A, tissue of origin absent. Lit., little. Mod., moderate. Mass., present in masses. Netw., present as a network. Conn. tiss., connective tissue. ? doubtful. B, beginning.

Chart 2.

Number.	Series.	Days.	Trabeculæ in			Absorption of			Connective-tissue hyperplasia of medulla.	In periosteum.	Between fragments.	In medullary cavity.	Apparent union.	Dense connective tissue between fragments.
			Periosteum.	Between fragments.	Medullary cavity.	Periosteal trabeculæ.	Medullary trabeculæ.	Cortex.						
19	2	21	+	—	+	+	?	+	+	+	+	+	Some mobility.	+
20	2	33	+	—	+	+	+	+	.	+	—		+	+
21	2	57	+	—	+	+	+	+		+	+		+	+
22	2	63	+	—	+	+	+	+	+	+	—		+	+
23	2	85	+	Few.	+	+	—	+	+	+	+	+	+	—
24	2	88	+	—	+	+	+	+	+	+	+	+	Very slight rocking.	—
25	2	129	+	+	+	+	+	+	+	—	—		+	—
26	2	262	+	+	+	+	+	+	?	+	+	—	+	—
27	2	277	+	+	+	+	+	+	?	+	+	—	+	+

Explanation: + present. — absent. ? doubtful. ▽ wedge-shaped.

parallel to the line of the original bone (Fig. 8). There is considerable absorption of the cortex and the medullary trabeculæ.

The tendons acted as a barrier to the formation of callus, forming grooves from which they had to be dug to release them.

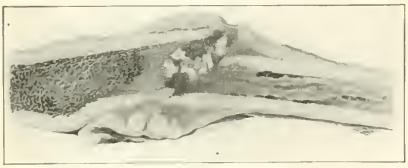

Fig. 5.—Experiment 20, Series 2, fracture thirty-five days. A drawing illustrating a fracture with slight lateral displacement. The cartilage is present in the form of islands across the line of fracture, and not as a wedge.

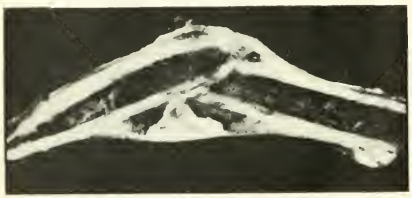

Fig. 6. Experiment 21, Series 2, fracture fifty-eight days. Illustrates a fracture with considerable angular displacement having abundant callus with a large wedge of cartilage on the internal aspect of the angle.

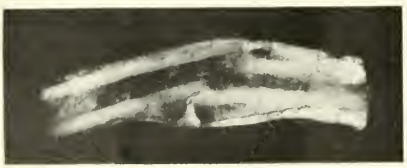

Fig. 7.—Experiment 22, Series 2 fracture sixty-three days. Illustrates a fracture with but slight angular displacement having a small wedge of cartilage on the periosteal aspect of the callus.

Microscopically, osteoid trabeculæ do not appear between the cortical ends of the fragments until the eighty-fifth day, and then in very small amount only, continuous with the medullary trabeculæ. Islands of cartilage are intermingled with them across the line of fracture. In a fracture of one hundred and twenty-nine days, in which there was very good position of the fragments, there is an entire absence of cartilage with great absorption of all the trabeculæ, the large spaces being again lined with a new deposit of bone which resembles the lamellæ of the old cortical bone, the cells being more spindle in shape than in ordinary osteoid tissue and the bone appearing denser in nature (Fig. 9). That new deposit is probably true osseous tissue. There are osteoid trabeculæ in between the cortical ends of the fragments which exhibit great absorption; also a deposit of new bone and union of the Haversian spaces of the old cortical ends. The union of the fracture is approaching completion, but the new tissue is still very porous. In another specimen, also, two hundred and sixty-two days in duration, in which there was good apposition of the fragments, there is osteoid

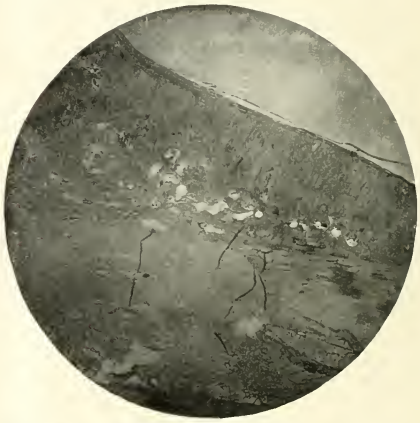

Fig. 8.—Experiment 21, Series 2, fracture fifty-seven days. Demonstrates the absorption that occurs in the deeper layers of the periosteal callus with the formation of spaces parallel to the cortex. This is part of the rearrangement or reorganization that occurs to accommodate for new conditions of stress and strain.

tissue between the ends of the cortical bone, it being denser, with more numerous and smaller spaces than the old cortical bone, which shows absorption. Its spaces communicate with the Haversian spaces of the old cortex. In this specimen the displacement was slightly greater than in the last one and there was, consequently, more cartilage present, the remnants of which are found in the periosteal callus as a very small wedge. Both the external and internal callus have undergone great absorption. In another specimen, two hundred and seventy-seven days in duration, there is still remaining a thin line of fibrocartilage at the site of the fracture, but not in the shape of a wedge. It is undergoing transformation into osteoid trabeculæ.

In this series the transition of cartilage into osteoid tra-

beculæ appears to occur in two different ways. It does not occur in the body of the mass of cartilage, as in the earlier stages of the development of callus (see Rabbit Experiments), but occurs only at the edge of the wedge (Fig. 10). Here the process appears to have a definite relation to the large osteoclasts which, in some cases, appear to invade the cartilage, absorb the ground substance, liberate the cells, and make way for the invasion of bloodvessels. This is to be followed by a deposition of lime salts on the borders of the cavities created, as in embryonal endochondral bone formation. In other areas, the deposit of lime salts appears to precede and then there is an invasion by bloodvessels and the formation of medullary spaces.

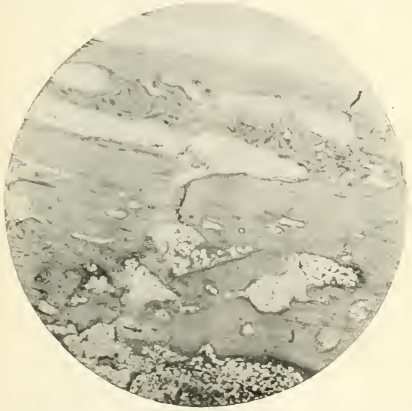

Fig. 9.—Experiment 25, Series 2, fracture one hundred and twenty-nine days. Illustrates the extensive absorption that occurs in the cortex and osteoid trabeculæ, followed by a deposition of new osseous tissue in the widened spaces. The new bone is seen as a very thin rim lining the dilated spaces (upper portion of figure).

This completes the two series in which complete subcutaneous fractures were studied with the object of investigating the subject as found clinically and with the object of confirming or denying the findings of other writers on the subject, particularly Dupuytren. Experiments performed in this manner, however, are unsatisfactory, for no two cases are under exactly similar conditions with reference to mobility, fragmentation, line of fracture, displacement, pressure from bandage, etc. There is no method of isolating the actually active portions of the bone and determining whether there is a definite reciprocal relation between the activities of the different factors of the bone. Each portion has been given credit for the chief or sole activity in the repair of fractures, and probably with much reason, because of the varying conditions of the specimens. In my own experiments as above described, while the general progression of the repair was more or less uniform, the comparative amounts of tissue from one or other portion of the bone varied in the different specimens. I think that experiments on rabbits are particularly unsatisfactory owing to the great difficulty in obtaining and maintaining good position of the fragments.

Having arrived at the above conclusion, the other series of experiments to be described were next carried out.

SERIES 3.

In this series the animals were placed under the influence of an anesthetic, an incision made over the inner aspect of the tibia down to the bone, and then a saw cut made in the bone until it penetrated the medullary cavity.

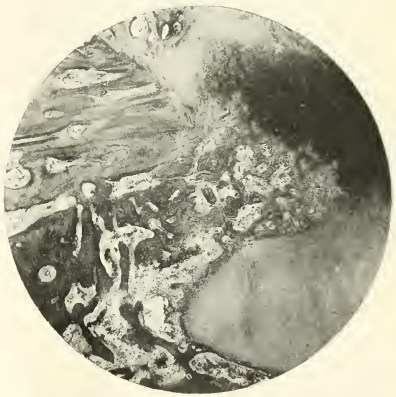

Fig. 10.—Experiment 21, Series 2, fracture fifty-seven days. Illustrates the transition of cartilage into osteoid tissue that occurs at the edge of the wedge of cartilage.

In this manner all portions of the bone were cut across and injured, but there were no extrinsic forces at work to influence union. The wound was immediately closed with silk sutures and the leg placed in a shaped wooden splint with a soda silicate bandage around it. The animals were killed at varying intervals from five to seventy days. Altogether, fourteen successful operations free from suppuration, etc., were obtained.

The specimen obtained at the end of five days exhibits no proliferation of the periosteum whatever, but in the medullary cavity there is an increase of the connective tissue between the fat cells which appears to obliterate them, for on the outskirts there can be noticed a gradual increase of the loose connective tissue with a commensurate decrease in the number

of fat cells. This new tissue is myxomatous in nature, many of the cells being typically stellate, others spindle with long, filamentous ends (Fig. 11). The substance between the cells is not very distinct, so that it is difficult to say whether this tissue is true myxomatous tissue or merely very loose connective tissue. The main point in favor of it being myxomatous in character, if not true myxoma, is the fact that on gross examination this tissue always resembles cartilage and has a glistening appearance. It was also quite firm. The new trabeculæ follow in the line of this new tissue. On the inner aspect of the cortex there is distinct thickening of the medullary membrane, with the formation of large polygonal cells which, in areas, appear to be secreting a homogeneous substance which takes the eosin staining.

Fig. 11 – Experiment 14, Series 4, fracture nine days. Shows the filamentous myxomatous character of the connective-tissue proliferation that occurs between the fat cells of the medulla.

This matrix becomes more abundant, the cells rearrange themselves in layers on its surface (some few being caught and imprisoned in it), and we have the formation of osteoid trabeculæ. Similar trabeculæ are forming on the spicule of bone that had been driven into the medullary canal by the saw. The sawcut is filled with blood clot and contains no formative cells.

At the end of seven days beginning signs of activity in the periosteum can be seen at some distance from the site of operation, there being proliferation of the deeper layers of the periosteum, with the production of the large formative cells in the osteogenetic layer. What appears to be more worthy of note is the fact that the periosteal surface of the cortex shows absorption by large polynuclear cells which are forming pits on the surface of the bone by the absorption of the lime salts. This, I believe, has considerable bearing on the future development of the periosteal osteoid trabeculæ. In the medullary cavity the process described under the last experiment is present to a greater degree, the formation of trabeculæ extending half-way across the medullary cavity and bridging over the wound in the bone. There is also a hyperplastic increase in the marrow, with the formation of red cellular marrow on the outskirts. With the exception of accentuation of the processes there is little change from the seventh to the ninth day, when the osteoid tissue in the medulla enters the sawcut and fills it about half the distance to the surface, the remainder being filled by fibroblasts and young bloodvessels with fibrin most superficial. The cortex proper, as well as its periosteal surface, begins to exhibit signs of slight absorption. There are no trabeculæ in the

Fig. 12. Experiment 32, Series 3, fracture ten days. Shows osteoid trabeculæ growing into the sawcut from the medulla (below), also absorption of the cortex along the sides of the cut.

periosteum and but slight proliferation except where there is superficial absorption of the cortex.

On the tenth day there is the first evidence of osteoid trabeculæ in the periosteum. In this particular specimen, in which there is more than the usual amount of inflammatory reaction, there is a fair amount of periosteal bone formation everywhere except at the margins of the sawcut, where it is absent. The sawcut is filled in with granulations into which osteoid trabeculæ are growing from the medullary trabeculæ (Fig. 12). In the medullary cavity there are osteoid trabeculæ surrounded by connective-tissue hyperplasia of the marrow, in which osteoid trabeculæ can be seen growing. This hyperplasia progresses from the edges of the new formation and occurs around groups of fat cells and not around individual cells, so that a scaffolding of connective-tissue trabeculæ is formed, upon which is con-

structed the trabeculæ formation (Fig. 13). The actual deposit of calcareous salts always begins from the cortex inward, that is, in contact with previous calcareous tissue. This specimen demonstrates clearly the method of trabeculæ formation from the periosteum, as described under the rabbit experiments, showing the two layers of the periosteum and the formation of the trabeculæ from the deeper layer. The trabeculæ nearest the cortex are thicker and the spaces between them smaller, proving that they had been formed first. There is increasing absorption of the cortex.

From the tenth to the seventeenth day little change is to be noted, there being no new developments, but merely an increase in all the elements noted above, viz., the periosteal, medullary, and sawcut trabeculæ. *All the trabeculæ in the sawcut are medullary in origin and course in a direction at right angles to the long axis of the bone.* They do not appear to have any attachment to the side of the bone until absorption of the sides of the sawcut occurs. The nutrient artery, instead of assisting in the formation of callus, can act as a barrier. In one specimen the trabeculæ follow along the artery for its entire length on the side of the fracture and are entirely absent on the other side.

Fig. 13.—Experiment 35, Series 3, fracture fifteen days. Demonstrates the formation of skeleton connective-tissue trabeculæ in the medulla by proliferation around and between groups of fat cells. It also illustrates how the osteoid trabeculæ grow into and along these trabeculæ of connective tissue (top).

As the periosteal trabeculæ increase, the general trend of the trabeculæ and of the spaces between the trabeculæ becomes very oblique, gradually becoming more and more in the general line of the bone. As early as the seventeenth day there is a certain amount of absorption of the deeper trabeculæ in a line with the old cortex, forming a space that runs almost parallel with the old cortex and just superficial to it, giving channels of communications with the spaces in the somewhat rarefied old cortex (Fig. 14).

The method of progression of the osteoid trabeculæ in the sawcut from the medulla to the surface is about as follows: The osteoblasts proliferate, elaborate a matrix, or cause modification in the tissue in which they lie. This is followed by a deposit of lime salts and the formation of the trabeculæ. These trabeculæ are covered by osteoblasts, some of which are in process of inclusion, being half in and half out of the osteoid mass (Fig. 15). From the seventeenth day absorption of the periosteal and endosteal trabeculæ occurs, but is more marked in the medullary tissue. Here great numbers

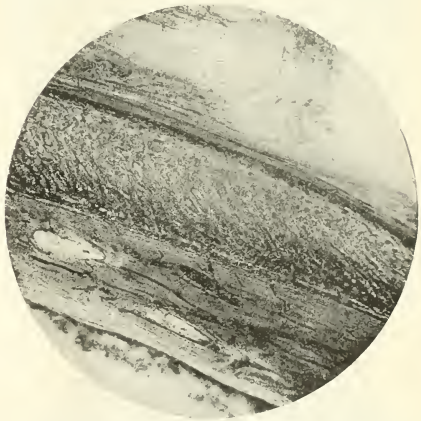

Fig. 14.—Experiment 37, Series 3, fracture seventeen days. Ground specimen. Shows the presence of a large amount of periosteal osteoid trabeculæ (above), the spaces between which communicate with the Haversian canals of the cortex. One long space runs superficial to and parallel with the cortex. The intertrabecular spaces are quite oblique in direction.

of large multinuclear cells with a large amount of protoplasm (Fig. 16) are to be found in relation with the trabeculæ, which show pits and depressions everywhere. Examination of the process under high powers demonstrates how the osteoclast opposes itself to the side of the trabeculæ and apparently dissolves out the calcareous salts and liberates the cells contained in them. These cells are not dead, but, as soon as released, the protoplasm again becomes evident, and the cell assumes a rounded shape, with a well-staining nucleus and a small amount of protoplasm, resembling in many respects the normal marrow cell. When liberated they do not look at all like the osteoblasts from which they were formed, but more like the small marrow cells from which, possibly, the original osteoblast dates its origin.

About this time absorption of the cortical sides of the sawcut, also, proceeds rapidly with the invasion of the trabeculæ in the sawcut and the establishment of communications between the spaces in the cortical bone and those between the trabeculæ in the sawcut. This is found in its earlier stages, when the general trend of the trabeculæ is still at right angles to the general line of the bone (Fig. 17). On the thirty-second day the osteoblasts have practically disappeared from the periosteal and medullary trabeculæ, demonstrating that their activity has practically ceased. There are no specimens in this series between the thirty-second and seventieth day, at which time a considerable change is noticed.

On the periosteal aspect of the seventy-day fracture there is a very compact, rather thick layer of new bone, which is continuous with the bone in the sawcut without a sign of a depression or break. Its outer layer exhibits consider-

Fig. 15.—Experiment 38, Series 3, fracture nineteen days. Demonstrates the method of formation of the sawcut trabeculæ, the osteoblasts being on the surface of the older trabeculæ, while they are in the process of inclusion in the younger forming trabeculæ, some of the cells being half within and half without the homogeneous osteoid mass

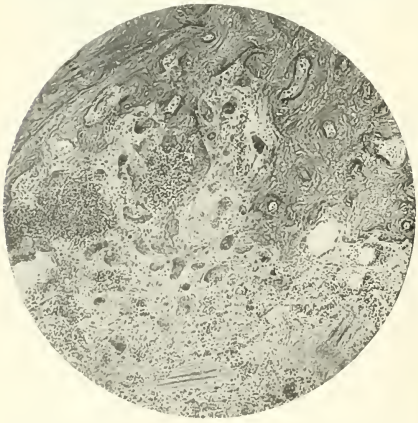

Fig. 16. Experiment 39, Series 3, fracture twenty-two days. Shows a large number of multinuclear osteoblasts which are causing extensive absorption of the medullary osteoid tissue. It also shows the cellular character of the marrow.

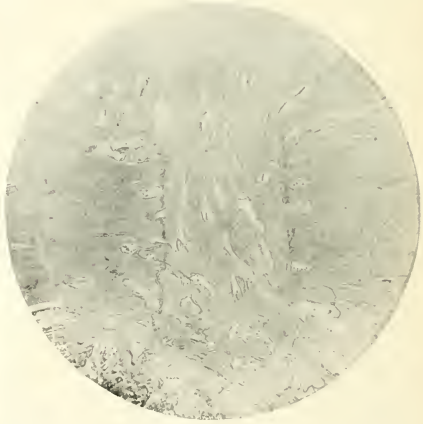

Fig. 17.—Experiment 39, Series 3, fracture twenty-two days. Demonstrates the vertical trend of the trabeculæ in the sawcut, absorption of the cortex on the sides of the cut and beginning communications between the new and old Haversian spaces.

able lacunar absorption. Here, as shown in Fig. 18, which is a wash drawing from a high power, photography being unsatisfactory, the process is practically similar to that which occurs in the medullary cavity. The osteoclast appears to dissolve out the lime salts and liberate the bone cells. What their fate is in this instance cannot be stated, as they cannot be found very far from the surface of the bone. They first appear as small round cells, with a moderate amount of protoplasm and well-staining nuclei. As they get farther away from the side of the bone they seem to get smaller and finally disappear. They probably degenerate, but of this I cannot be positive.

CHART 3.

Number.	Series.	Days.	Trabeculæ in			Osteoblasts on			Absorption of					Marrow.	Direction of medullary spaces between sawcut trabeculæ with reference to the axis of the bone.	Communications between old Haversian canals of cortex and those between sawcut trabeculæ.
			Periosteum.	Sawcut.	Medullary cavity.	Periosteal trabeculæ.	Medullary trabeculæ.	Cortex.	Periosteal trabeculæ.	Medullary trabeculæ.	Cortex.					
											Sawcut	Interstitial.	Surface.			
28	3	5	—	—	+	A	+	+	A	—	—	—	—	Pink.	A	A
29	3	7	—	—	+	A	+	—	A	—	—	—	+	Red.	A	A
30	3	8	—	—	+	A	+	—	A	—	—	—	+	Red.	A	A
31	3	9	—	½	+	A	+	—	. .	—	—	Sl.	+	Red.	L	—
32	3	10	+	Few.	+	+	+	—	—	—	+	+	+	Red.	L	—
33	3	11	+	+	+	+	+	—	—	?	—	+	—	Red.	L	—
34	3	12	+	Few.	+	+	+	—	—	—	+	+	+	Red.	L	—
35	3	15	+	+	+	+	+	—	—	—	—	+	+	Red.	L	—
36	3	16	Sl.	+	+	+	+	+	—	—	+	+	+	Red.	L	—
37	3	17	+	+	+	+	+	+	?	+	+	+	+	Red.	L	—
38	3	19	+	+	+	+	+	—	—	—	+	+	—	A	L	—
39	3	22	+	+	+	+	+	—	—	+	+	+	Sl.	Red.	L	+
40	3	32	+	+	+	. .	. .	. .	+	+	—	+	—	Red.	L	+
41	3	70	+	+	+	—	—	—	+	+	+	+	Sl.	Red.	—	+

Explanation. + present. — absent. A, primary tissue absent. Sl., slight. ½, half-way across. L, at right angles. — parallel. ? doubtful.

The sawcut is very interesting and instructive. It is entirely filled with more or less compact bone in which the trend of the medullary spaces between the trabeculæ has changed from at right angle to the line of the bone to a direction parallel with it (Fig. 19). Differences in staining show

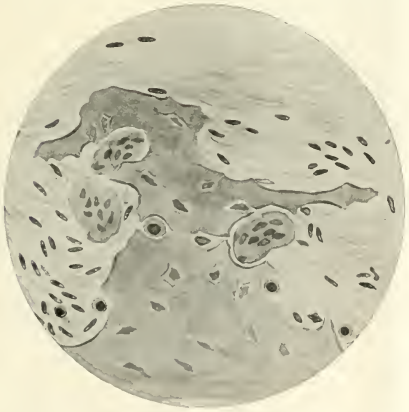

FIG. 18.—Experiment 41, Series 3, fracture seventy days. Wash drawing showing how the osteoclasts dissolve the calcium salts in the periosteal trabeculæ and free the bone cells which become lost in the connective tissue.

how the old vertical spaces had been filled in and new transverse spaces made which originally were very large. These new spaces communicated with similar spaces in the old cortex. This was followed again by a deposition of new bone which was continuous throughout the new space, forming a firm bond of union between the old cortex and the new trabeculæ. The new deposit is in the form of lamellæ and the cells in them more of the normal spindle shape of bone cells. Thus we see that under conditions where no extrinsic forces have been at work the process of repair is practically complete at the end of seventy days, showing further progress than the complete fractures did at the end of two hundred and sixty-two days. In addition, there is not the slightest suggestion of cartilage in any of the specimens.

SERIES 4.

While Series 3 isolated to a greater or less extent the activities of the different portions of the bone and demonstrated their various activities, the other series were performed to ascertain whether the activities of one portion could be substituted for those of another. In Series 4 the action of the medulla and cortex, without the assistance or influence of the periosteum, was studied. The animals were placed under the influence of an anesthetic and an incision made over the inner aspect of the tibia. The bone was denuded of periosteum for about one to one and a half inches in the region of the operation, and the periosteum cut off. A sawcut was then made in the bone sufficiently deep to enter the medullary cavity. The wound was sutured and a splint applied with a sodium silicate bandage.

The results in this series correspond very closely to those of the previous series with reference to the activities in the bone and medulla, with the exception that these seem to be somewhat increased. The absorption that occurs in the cortex begins early and is more marked than in the case where the periosteum was intact. The sawcut is filled in the same manner as (and, if anything, slightly sooner than) in

the last experiment, since by the twelfth day it is completely filled in and "overflows" the edge of the cut, appearing to a small extent on the periosteal aspect of the cortex. The communications between the dilated cortical spaces and the spaces between the trabeculæ in the sawcut are established much sooner, being present as early as the twelfth day. The medullary trabeculæ fill the sawcut so rapidly that by the nineteenth day they extend well over the periosteal surface of the cortex and "overflow" upon it (Fig. 20). They also fill in the normal dilated cancellous spaces in the cortex that have been cut across.

Absorption of the cortex proceeds rapidly and is extensive in the region of the sawcut (Fig. 21) in marked contrast to the remainder of the bone.

The healing of the defect progresses so rapidly that the absorption of the medullary trabeculæ begins as early as the twelfth day, whereas in the previous series it did not begin until the seventeenth day. Absorption of the surface

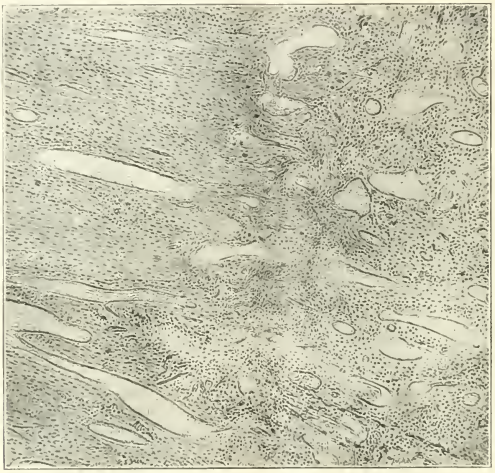

Fig. 19.—Experiment 41, Series 3, fracture seventy days. Demonstrates how the spaces between the trabeculæ in the sawcut change from a vertical to a horizontal direction parallel with the line of the bone, and how they unite with the Haversian spaces of the cortex, this being followed by a deposit of new bone in the two. Three stages of bone formation can be seen. Old cortex to left and sawcut to right of picture.

Chart 4.

Number.	Series.	Days.	Trabeculæ in			Osteoblasts on			Absorption of					Marrow.	Direction of medullary spaces between sawcut trabeculæ with reference to the axis of the bone.	Communications between old Haversian canals of cortex and those between sawcut trabeculæ.
			Periosteum.	Sawcut.	Medullary cavity.	Periosteal trabeculæ.	Medullary trabeculæ	Cortex.	Periosteal trabeculæ.	Medullary trabeculæ.	Cortex.					
											Sawcut	Interstitial.	Surface.			
42	4	5	A	Few.	Few.	A	—	—	A	—	—	+?	—	Red.	L	—
43	4	7	A	Few.	Few.	A	+	—	A	—	+	+	—	Red.	L	—
44	4	9	A	+	—	A	+	?	A	—	—	—	—	Red.	?	?
45	4	12	A	Few	+	—	+	—	+	—	+	+	+	Red.	L	+
46	4	15	A	+	+	A	+	—	A	+	+	+	+	Pink.	L	Beginning.
47	4	19	A	+	—	+	+	—	—	+	—	+	+	Red.	L	—
48	4	23	A	+	—	A	—	+	A	+	+	+	+	Red.	L	+
49	4	28	A	+	+	+	—	+	+	+	+	+	+	Red.	L	+
50	4	49	A	+	+	A	—	+	A	+	+	+	+	Pink.	—	+

Explanation: + present. — absent. A, primary tissue absent. ? doubtful. L, at right angles. ‖ parallel.

of the cortex is not found until the twelfth day, but it continues throughout the remainder of the experiments, until the forty-ninth day, in contrast with the previous series, in which it almost ceases at the end of the seventeenth day. Osteoblasts disappear from the surface of the medullary trabeculæ by the forty-ninth day, but are present in the cortex from the twenty-third to the forty-ninth day.

Fig. 20.—Experiment 47, Series 4, fracture nineteen days. Illustrates the sawcut filled with medullary trabeculæ "overflowing" the periosteal side (above) of the cortex where the periosteum had been denuded. They also fill a normal cancellous space in the cortex (right).

Fig. 21.—Experiment 48, Series 4, fracture twenty-three days. Ground specimen. Shows extensive absorption of the cortex in the region of the sawcut (left) with a tendency for these dilated spaces to unite with the spaces between the medullary osteoid trabeculæ (below).

The specimen from a forty-nine days' fracture shows the first stages in the change of direction in the medullary spaces between the sawcut trabeculæ. As in the last experiment of the previous series, the old spaces are being filled in and new spaces, lined with osteoblasts, are being formed, communicating with similar spaces in the old cortex (Fig. 22). The marrow, in all the experiments of the series, is hyperplastic with an increase in cellular content. In almost all of the specimens the periosteum, where it was still attached at the point of excision, shows a liberal amount of new bone. On the opposite side of the bone there is lacunar absorption and a proliferation of the osteoblastic layer of the periosteum without the formation of bone

Fig. 22.—Experiment 50, Series 4, fracture forty-nine days. Ground specimen. Shows extensive absorption of the sides of the sawcut creating spaces which unite the Haversian canals of the cortex with the spaces between the trabeculæ in the sawcut.

SERIES 5.

The method of operating for the performance of this series of experiments was identical with that for Series 4, with the exception that the sawcut was superficial and did not enter the medullary canal. Thus, with the periosteum removed and the medulla not disturbed the activity of the cortex could be determined. Eight successful specimens have been obtained. The results, in brief, of this series are as follows:

Absorption of the cortex proper is the most constant result. It is present to a very marked degree in all the specimens and increased in quantity, depending on the depth of the sawcut. In only one specimen (a fracture of twelve days' duration) were there any periosteal trabeculæ in the region of the wound. It is probable that in this case the entire periosteum was not removed, but merely the fibrous

layer. In almost all of the specimens the medulla shows signs of irritation in the increased cellular content of the marrow. In four of the eight specimens there is a growth of osteoid tissue in the medullary cavity. The extent of this growth depends more on the depth of the sawcut and the extent to which absorption of the cortex had progressed than upon the duration of the fracture (Figs. 23 and 24).

Fig. 23.—Experiment 54, Series 5, fracture twenty-four days. Shows a shallow sawcut filled with proliferated connective tissue and blood clot, moderate absorption of the cortex and a moderate amount of osteoid tissue on the medullary aspect of the cortex (below).

This growth occurs as a smooth, well-defined elevation, from the inner aspect of the cortex, unaccompanied by considerable hyperplastic increase of connective tissue in the marrow, but, especially in one specimen (Fig. 24), by the condensation of the tissue in the region of the growth with the formation of a membrane almost similar to the deeper layer of the periosteum. *In none of these specimens is there a diffuse increase of connective tissue in the marrow, with the formation of the skeletal trabeculæ, and in none of the experiments is there an irregular deposit of osteoid trabeculæ.*

In four of the experiments the sawcut contains osteoid tissue. It appears first on the twelfth day, as a small

Fig. 24.—Experiment 53, Series 5, fracture twelve days. Illustrates the large amount of medullary osteoid tissue that is associated with a deep sawcut (upper left-hand corner) and absorption of the cortex. The medullary trabeculæ are limited by a membrane that resembles the deeper layer of the periosteum.

amount of thin trabeculæ at the base of the cut, showing no general direction to the spaces, which are large and rounded. There is a great amount of absorption of the cortex and a large mass of trabeculæ in the medullary canal.

Chart 5.

Number.	Series.	Days.	Trabeculæ in			Osteoblasts on			Absorption of						Direction of medullary spaces between the sawcut trabeculæ with reference to the axis of the bone.	Communications between old Haversian canals of cortex and those between sawcut trabeculæ.
			Periosteum.	Sawcut.	Medullary cavity.	Periosteal trabeculæ.	Medullary trabeculæ.	Cortex.	Periosteal trabeculæ.	Medullary trabeculæ.	Cortex. Sawcut.	Cortex. Interstitial.	Cortex. Surface.	Marrow.		
51	5	3	A	—	—	A	—	+	A	A	—	+	—	Sl. con.	A	A
52	5	5	A	—	—	A	A	—	A	A	—	?	—	A	A	A
53	5	12	A	+	+	+	+	—	—	—	+	+	—	Pink.	Indifferent.	+
54	5	24	A	+	+	A	A	+	A	A	—	+	—	Red.	A	A
55	5	30	A	+	—	A	?	?	A	—	+	+	—	Red.	— ?	— ?
Ground.																
56	5	35	A	—	—	A	A	+	A	A	+	+	?	Red.	A	A
57	5	45	A	+	+	A	?	?	A	?	—	+	?	Red.	—	+
Ground.																
58	5	70	A	+	+	A	—	—	A	+	+	+	+	Red.	Indifferent.	+

Explanation: + present. — absent. A, primary tissue absent. ? doubtful. Sl. con., slight congestion. = parallel.

A ground specimen from a fracture of thirty days also exhibits a similar condition, but in this case there is not so much absorption of the cortex. A specimen from a thirty-

Fig. 25.—Experiment 57, Series 5, fracture forty-five days. Ground specimen. Illustrates the extensive absorption of the cortex that occurs near a shallow sawcut, especially between it and the medullary cavity.

Fig. 26.—Experiment 58, Series 5, fracture seventy days. The sawcut (above) is filled with new compact bone, which is undergoing lacunar absorption upon its surface. There is marked absorption of the cortex with a tendency to the formation of communications between the cortical and new bone spaces. There is some new bone formation in the medullary cavity.

five-day fracture does not contain trabeculæ in the sawcut, but in this case the injury was very shallow and the development of all the stages of the process has been very slow. There is a small amount of osteoid tissue in the medullary cavity, and also absorption.

A specimen from quite a deep fracture of forty-five days' duration shows marked response in all portions of the bone. There is considerable absorption of the cortex, with a large amount of osteoid trabeculæ in the medullary cavity and in the sawcut (Fig. 25). A similar condition is found in a fracture of seventy days' duration (Fig. 26), with the exception that most of the medullary trabeculæ are absorbed and the surface of the trabeculæ in the sawcut is undergoing lacunar absorption (Fig. 27). In both of these specimens there is no definite direction to the spaces between the trabeculæ, but the general trend is more in the line of the bone than transversely. Throughout this series there is practically no absorption of the periosteal surface of the cortex.

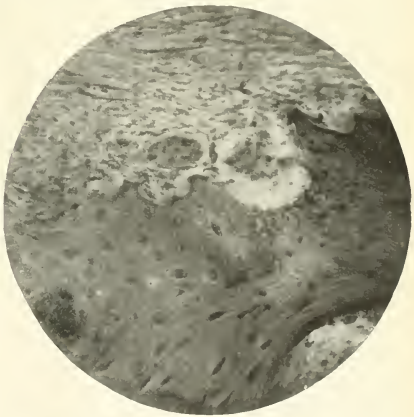

Fig. 27.—Experiment 58, Series 5, fracture seventy days. A high-power photomicrograph of the lacunar osteoclastic absorption seen upon the surface of the last specimen. It shows the liberation of bone cells.

SERIES 6.

This series, performed upon dogs, had as its object the determination of the activity of the periosteum when raised from the bone, associated with injury to the bone itself, not deep enough to enter the medullary canal. Each operation consisted in exposing the inner side of the tibia, raising the periosteum, and, in some instances, cutting one end of the raised periosteum, and, in other instances, raising the periosteum without cutting it transversely. The bone was then injured superficially with rongeur forceps or shallow sawcuts. Where the periosteum had been cut transversely it was sutured in place with catgut, and where this transverse section had not been made it was merely allowed to fall back into place. The wound was then sutured and covered with collodion.

Ten successful specimens were obtained, the duration of the injuries ranging from two to forty-nine days. The results in this series, while not perfectly uniform, all tend in the same direction. After the eighth day they exhibit proliferation of the periosteum and bone formation, with the exception of the cases in which the raised periosteum had not again adhered to the cortex. Here the periosteum is proliferated with an apparent effort at trabecular formation, but there is no deposit of calcium salts in them. The proliferated periosteum dips into the sawcuts and in some of the specimens has apparently proceeded to form new bone. Whether this new bone in the base of the sawcut is always derived from the periosteum or from the medullary tissue in the cortex, as in the experiments of Series 5, it is impossible to state, for there are no trabeculæ in the sawcuts where there is no absorption of the cortex and lining of osteoblasts in its dilated spaces. The only apparent exception to this is Experiment 68, forty-nine days in duration. Here the process was probably already complete and the spaces filled in.

Particular attention is called to the fact that wherever there has been the formation of osteoid tissue in the raised periosteum upon the superficial surface of the cortex, there also has been superficial lacunar absorption of the cortex. In most of the cases there is also absorption of the cortex proper.

Chart 6.

Number.	Series.	Days.	Proliferation of deeper layers of raised periosteum.	Osteoid trabeculæ in the raised periosteum.	Trabeculæ in medullary cavity.	Marrow.	Absorption of cortex.			Osteoblasts in cortex.
							Sawcut.	Interstitial.	Surface	
59	6	2	—	—	—	Pink.	—	—	—	?
60	6	3	—	—	—	Red.	—	+	?	+
61	6	4	—	—	—	Red.	—	+	—	Bone cells.
62	6	8	+	+	+	Red.	+	+	+	+
63	6	10	+	+	—	Cong.	+	+	+	+
64	6	14	+	+	—	Pink.	+	—	+	—
65	6	19	?	—	+	Pink.	—	+	+	+
66	6	29	Slight.	+	+	Pink.	+	+	+	+
67	6	38	Moderate.	+	—	Pink.	+	+	+	?
68	6	49	Moderate.	+	+	Red.	—	+	+	—

Explanation: + present. — absent. ? doubtful. Cong., congested.

In all the specimens the medulla is cellular, in some to a greater extent than in others. Whether this fact is due to the operation or normal to the animal operated upon it is impossible to state, but the fact that, in some of the specimens, the marrow is more cellular toward the cortical edges and yellow in the centre appears to point to some influence upon it of the injury to the bone. Six sections of this series contain large multinuclear cells with abundant protoplasm. They are identical in appearance with osteoclasts, but whether they are osteoclasts or myelocytes it is impossible to prove. Indeed, the two may be identical in fact as well as in appearance. In two specimens in particular (Experiments 60 and 61) there was a condition in the marrow that seems to point to the origin of these multinuclear cells. The medulla of Experiment 60 contains cells of varying sizes: some small round cells with deeply staining nuclei (occasionally eccentrically placed), others with larger vesicular nuclei, and, finally, very large cells with an abundance of protoplasm and four to ten rather large, vesicular nuclei. The medulla of Experiment 61 contains numerous round or oval cells of varying size, with small or moderate-sized, round, well-staining nuclei which, especially toward the ends of the bones, exhibit slight increase in protoplasm and an apparent division of the nuclei into two or four parts.

In four of the experiments there was a formation of osteoid tissue in the medullary cavity, usually moderate in amount, and only in cases where the sawcuts were quite deep. Experiment 68 would appear to be an exception, since the celloidin sections contain a large amount of trabeculæ in the medullary cavity and shallow cuts. In this case the section retained for grinding probably demonstrated the cut to have been quite deep. However, as the specimen was not ground, this is offered merely as an assumption and not as a fact. In a specimen from an experiment of thirty-eight days' duration the defect in the bone is filled in by osteoid trabeculæ, the spaces between which communicate with the spaces caused by absorption of the old cortex.

Series 7.

In this series an effort was made to determine whether an animal substance (catgut) placed under the periosteum would excite the formation of bone when not associated with injury to the cortex. The periosteum was raised by an incision along the side of the bone and a coiled strand of No. 2 catgut slipped under it. The wound was then sutured. There were but two operations in this series, and there is a microscopic description of only one of these. In both the macroscopic and microscopic sections there was no new bone formation under the raised

periosteum. Microscopically, the catgut is seen to be encapsulated by fibrous tissue and is undergoing partial absorption by leukocytes. Under the portion of the periosteum that still remains attached there is a thin deposit of quite dense new bone which is undergoing absorption on its superficial surface. There is no new bone formation in the medullary cavity, but there is some superficial and slight interstitial absorption of the cortex.

SERIES 8.

This consisted of one successful operation, fifty-one days in duration, in which the periosteum was raised and celloidin, hardened in bichloride alcohol, placed under it to determine if an unabsorbable material would excite bone formation. The celloidin must have slipped from underneath and worked its way above the periosteum, as seen by the microscopic sections. The periosteum shows cellular proliferation, but there is no osteoid bone formation. There is some superficial but little interstitial absorption of the cortex. The marrow is red, but there are no osteoid trabeculæ in the medullary cavity.

SERIES 9 AND 10.

Each consisted of one operation in which the periosteum was raised without injury to the cortex and allowed to fall back into place. In one there was no effort made at hemostasis in the hopes of having a clot form under the periosteum. In the other hemostasis was as perfect as possible.

The results are the same in both. There is superficial absorption of the cortex by osteoclasts, slight cellular proliferation in the periosteum, but no signs of osteoid bone formation. There is but slight, if any, interstitial absorption of the cortex. The marrow of injured and uninjured bone is red and shows large multinuclear cells.

SERIES 11, 12, 13 AND 14.

These four series are treated together because of the close relationship they bear to one another and because they all have as their object the determination of the action of different conditions upon regeneration, after subperiosteal resection of the tibia according to Nichols' method.

The basis of the operations was a typical subperiosteal resection of the tibia performed in the usual manner, by raising the periosteum and removing a section of bone about one inch in length; then of bevelling off the ends of the fragments to obliterate dead spaces, and, finally, suturing the two surfaces of the periosteum together throughout the entire length of the defect. The different series each consisted of two operations upon dogs and were varied in the following manner:

In Series 11 a thin strip of tibia was left connecting the two ends of the fragments and making a bridge between them. The periosteum was sewed over that.

Series 12 consisted of a typical subperiosteal resection.

In Series 13 the medulla was removed from the bone and placed in salt solution, and, after the remainder of the cortex had been removed, was sutured between the two surfaces of the periosteum.

In Series 14 thin strips of dried bone were sutured between the layers of the periosteum.

The fractures of the first three series (excepting Experiment 78) were between forty-four and fifty-two days in duration, so that their results can be readily compared. The two of the last series were eight and twenty-nine days in duration.

Macroscopically, in all but the two last operations there was a moderate amount of firmness to the legs in spite of the fact that in several the fibula had been fractured, but reunited to a great extent.

With reference to the amount of osteoid tissue thrown out, as studied by the radiograph, we find in Series 11 (Figs. 28 and 29) a very moderate deposit of new bone over the bridge of tissue connecting the two ends of the fragments and over the ends of the fragments across the medullary canal. With the exception of a small isolated island of osteoid tissue in one, the defect in the bone appears to be devoid of any calcium salts in the form of trabeculæ and appears perfectly clear in the negative.

Series 12 (Figs. 30 and 31) and Series 14 (Figs. 32 and 33) correspond in their results, in that in neither is there any new bone formation excepting at the ends of the fragments of the tibia and across the medullary canals.

The two specimens from Series 13, in which the medulla was replaced between the layers of periosteum, exhibit a remarkable exception to the above results. The radiograph from Experiment 78, which was only thirty-one days in duration (Fig. 34), although taken at an incorrect angle so that the tibia overlaps the fibula, nevertheless demonstrates clearly a bridge of osteoid tissue extending from one fragment to the other. Its depth cannot be properly estimated from the picture, but microscopic and longitudinal sections show it to be considerable. The most remarkable radiograph is from Experiment 79, which was a fracture of fifty-two days' duration (Fig. 35). Here we see the defect in the tibia more than completely filled by osteoid tissue, so that it is thicker than the bone itself. It is broken by a couple of light streaks which, on cross-section, are found to be cartilage. The animal had perfect use of the leg, which in all respects was absolutely firm.

Longitudinal sections, in all cases, confirm the *x*-ray findings with reference to the new bone formation, but showed that in most of the cases the light areas between the ends of the fragments consisted of cartilage or dense connective

tissue, which in some instances was found to be fibrocartilage.

The microscopic sections serve to accentuate some portions of the process that are not brought out by the gross examinations. Foremost is the fact that in almost every instance there is a thin lid or cap of osteoid tissue covering the exposed ends of the medullary cavity of the fragments of the tibia. The process of osteoid bone formation does not appear to extend far up into the cavity. The marrow

Fig. 28.—Experiment 74, Series 11, fracture forty-seven days. Radiogram. Partial superiosteal resection. There is a thin deposit of new bone along the bridge of old cortex, connecting the two fragments of tibia and some over the ends of the fragments. The fibula had been fractured and united with abundant callus.

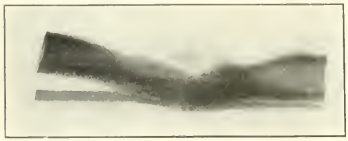

Fig. 29.—Experiment 75, Series 11, fracture forty-four days. Radiogram. Partial subperiosteal resection. There is a deposit of new bone upon the bridge of old cortex connecting the two fragments of tibia, also an isolated island of new bone between the fragments.

Fig. 30.—Experiment 74, Series 12, fracture forty-six days. Radiogram. Typical subperiosteal resection. There is dislocation of one of the fragments of the tibia. There is no new bone filling in the defect. The fibula is fractured and there is abundant callus upon the fragments.

is more cellular than usual, especially near the ends, but not as cellular as in the experiments of previous series. The ends of the bone almost invariably show lacunar absorption by osteoclasts. There is usually, also, a moderate osteoid deposit on the periosteal side of the fragments.

Cartilage is the dominant tissue filling the defect in the tibia. It is either hyaline cartilage or fibrocartilage. The hyaline cartilage is usually found nearer the ends of the fragments or in relation with forming osteoid trabeculæ. Cartilage is even found in Experiment 79, but here it is in

Fig. 31.—Experiment 77, Series 12, fracture forty-four days. Radiogram. Typical subperiosteal resection. There is no new bone filling in the defect of the tibia.

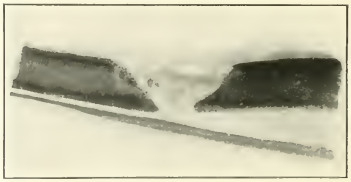

Fig. 32.—Experiment 80, Series 14, fracture eight days. Radiogram. Typical subperiosteal resection of tibia with reposition of bone salts. There is some evidence of the thin section of bone which was sutured between the layers of the periosteum, but no new bone formation in the defect of the tibia.

Fig. 33.—Experiment 81, Series 14, fracture twenty-nine days. Radiogram. Typical subperiosteal resection of tibia with reposition of bone salts. There is no new bone formation filling in the defect of the tibia. There is a fracture of the fibula with angular displacement.

the form of narrow strips surrounding large masses of spongy osteoid tissue. They are evidently the remnants that are undergoing conversion into osteoid tissue.

In these experiments the conversion of cartilage into osteoid tissue more closely resembles embryonal bone formation

or that seen at the epiphyseal ends of a growing bone than that in any of the previous series. The cartilage near the ends of the fragments, usually hyaline in character and often taking a very blue stain, most frequently undergoes a rather

FIG. 34. Experiment 78, Series 13, fracture thirty-one days. Radiogram. Typical subperiosteal resection of tibia with reposition of medulla. The tibia partially overlaps the fibula, which is intact. There is a fair-sized growth of new bone connecting the two fragments of the tibia, and partially filling the spaces from which the section of tibia had been removed.

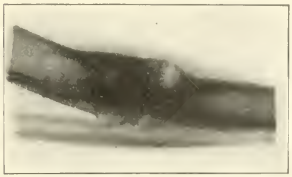

FIG. 35.—Experiment 79, Series 13, fracture fifty-two days. Radiogram. Typical subperiosteal resection of tibia with reposition of medulla. The defect in the tibia is filled with an abundant growth of osteoid tissue, which is partially divided by a strip of cartilage (light streak). The fibula is intact.

CHART 7.

Number.	Series.	Days.	Trabeculæ in			Absorption of cortex.			Osteoblasts in cortex.	Marrow.	Direction of medullary spaces between sawcut trabeculæ with reference to the axis of the bone.	Communications between old Haversian canals of cortex and those between sawcut trabeculæ.
			Periosteum.	Sawcut.	Medullary cavity.	Sawcut.	Interstitial.	Surface.				
59	6	2	—	—	—	—	—		—	Pink.	A	A
51	5	3	A	—	—	—	+	—	+	Sl. cong.	A	A
60	6	3	—	—	—	—	+	?	+	Red.	A	A
61	6	4	—	—	—	—	+		Bone cells.	Red.	A	A
28	3	5	—	—	+	—	—	—	+	Pink.	A	A
42	4	5	A	+	+	—	+	—	—	Red.	L	—
52	5	5	A	—	—	—	+	—	+	Sl. cong.	A	A
29	3	7	—	—	+	—	—	—	+	Pink.	A	A
43	4	7	A	+	+	?	+	—	—	Red.	L	—
30	3	8	—	—	+	—	—	+	—	Red.	A	A
62	6	8	+	Beg.	+	+	+	+	+	Red.	Indifferent.	
31	3	9	—	½	+	—	Sl.	+	—	Red.	L	—
44	4	9	A	+	+	—	—	—	?	Red.	.....	?
32	3	10	+	Few.	+	+	+	+	—	Red.	L	—
63	6	10	+	Beg.	—	+	+	+	+	Congested	Indifferent.	
33	3	11	+	+	+	—	+		—	Red.	L	
34	3	12	+	Few.	+	+	+	+	—	Red.	L	—
45	4	12	A few.	+	+	+	+	+	+	Red.	L	+
53	5	12	A +	+	+	—	+	—	—	Pink.	Indifferent.	+
64	6	14	+		—	+	—	+	—	Pink.	A	A
35	3	15	+	+	+	—	+	+	—	Red.	L	—
46	4	15	A	+	+	+	+	+	—	Pink.	L	Beginning.
36	3	16	Sl.	+	+	+	+	+	+	Red.	L	—
37	3	17	+	+	+	+	+	+	+	Red.	L	—
38	3	19	+	+	+	—	—	—	—	A	L	—
47	4	19	A +	+	+	—	+	+	—	Red.	L	—
65	6	19	—	—	+	—	+	+	+	Pink.	A	A
39	3	22	+	+	+	+	+	Sl.	—	Red.	L	+
48	4	23	A	+	+	+	+	+	+	Red.	L	+
54	5	24	A	—	+	—	+		+	Red.	A	A
49	4	28	A +	+	+ +	—	+	+	+	Red.	L	+
66	6	29	+	+	+	+	+	+	+	Pink.	Indifferent.	+
55	5	30	A	?	—	+	+	—	?	Red.	?	?
Ground.												
40	3	32	+	+	+	—	+	—	—	Red.	L	+
56	5	35	A	—	+	+	+		+	Red.	A	A
								d. f. e.				
67	5	38	+	+	—	+	+	+	?	Pink.	—	+
57	5	45	A	+	+	—	+	?	?	Red.	—	+
Ground.												
50	4	49	A	+	+	—	+		+	Pink.	—	+
68	6	49	+	+	+	—	+	+	—	Red.	—	+
41	3	70	+	+	+	+	+	—	—	Red.	—	+
58	5	70	A	+	+	+	+	+	—	Red	—	+

Explanation: + present. — absent. A, primary tissue absent. ? doubtful. Beg., beginning. Sl. cong., slightly congested. ½, half its depth. Sl., slight. d. f. e., distance from cut. L, at right angles. = parallel.

marked change, the cells becoming arranged in rows or columns with narrow strips of clear matrix between them. Then there is absorption of this matrix and a penetration by bloodvessels. At the same time there is calcification of the remaining narrow strips of cartilage. This is followed by a deposition of more osteoid tissue in lamellæ. The latter tissue takes a deep-red stain and very closely resembles true osseous tissue. This is the typical appearance of almost all the trabeculæ, viz., a central portion containing cells irregularly disposed and taking a bluish stain, and an outer portion consisting of several lamellæ of dense tissue with an orderly arrangement of the cells, the whole taking a deep-red eosin stain. In the experiments of Series 13 the spaces between the trabeculæ filling in the defect in the bone are exceptionally vascular, containing many thin-walled bloodvessels and much free corpuscular blood. The marrow contained in them is very cellular. This is the fact that appears as if it may have direct bearing upon the influence exerted by the medulla placed between the layers of the periosteum. This cellular marrow contains abundant osteoclasts which have, throughout the experiments, appeared to be in close connection with the early deposition of osteoid trabeculæ. They are evidently medullary in origin and may be abundant in these spaces because they may have developed in their present situations.

The experiment of eight days of Series 14 was very interesting from the microscopic standpoint. The centre of the defect is filled with blood clot, but toward the ends of the fragments of the tibia it is replaced by cellular connective tissue, which appears to take origin from the medulla. It contains many round or oval cells that resemble closely the normal marrow cells. It is quite vascular, the vessels also appearing to come from the marrow, which is very vascular. The endosteum and periosteum have already given rise to osteoid trabeculæ on the internal and external aspect of the cortex.

The section of bone placed between the layers of the periosteum shows slight absorption in places, but no deposition of new bone on its surface. This may be of some significance in showing the necessity of the presence of living bone cells in order to have a deposition of bone upon loose fragments. In all the specimens of all the series the cortex exhibits very marked absorption.

The fibula has also shared in the activities of the bone even in cases where it was not fractured. The cortex invariably exhibits absorption to a marked degree, and there is frequently a deposition of osteoid trabeculæ even in the absence of fracture. Where there is not an actual deposit of bone, there is marked superficial lacunar absorption of the cortex and proliferation of the deeper layers of the periosteum.

The striking feature of the results of these experiments is the remarkable growth of osteoid tissue filling the defect of the tibia of those cases in which the medulla was replaced between the layers of the periosteum.

COLLECTIVE REVIEW OF SAWCUT EXPERIMENTS.

Reviewing collectively (Chart 7) all the sawcut experiments, that is to say, the experiments in which the conditions governing repair could be definitely controlled, we find that the first sign of activity on the part of the bone occurs in the form of absorption of the cortex. This is found on the third day in Experiment 51, Series 5, and Experiment 60, Series 6. The probable reasons why this is the earliest activity noticed are that none of the experiments in which the sawcut entered the medulla were shorter in duration than five days, and that in both the experiments mentioned the periosteum had been removed from the bone, although in one case it was allowed to fall back into place.

When we come to the fifth day we are struck with the fact that in those experiments in which the medullary cavity had been entered there is present in it a new formation of osteoid tissue (Experiments 28 and 42). This appears to be greater in amount in the experiments in which the periosteum has been removed from the bone than in those in which it is left remaining. In the former (Series 4) the medullary trabeculæ enter the sawcut as early as the fifth day, whereas in the latter this does not occur until the ninth day.

Absorption of the sides of the sawcut does not appear until the eighth day (Experiment 62) and does not seem to bear any definite relation to the form of experiment performed. It is not constant in its occurrence.

The most important factor that can be noted when considering these experiments is that, with but two exceptions in Series 5, where the periosteum was removed and only shallow sawcuts made in the bone, and two exceptions in Series 6, where the periosteum was raised from the bone and shallow cuts made, the sawcut in every experiment after the eighth day contains osteoid trabeculæ. In *every* operation in which the medullary cavity has been entered the trabeculæ in the sawcut take origin in the medullary canal. In every experiment up to the thirty-second day, in which the medullary cavity has been entered and there are trabeculæ in the sawcut, the direction of these trabeculæ is at right angles to the axis of the bone. In those experiments in which the medullary cavity has not been entered there is usually no definite direction to the trabeculæ, the spaces between them being round.

In every experiment after the thirty-eighth day, in which there are trabeculæ in the sawcut, the direction of the spaces and trabeculæ is in the line of the bone, and there are communications between the spaces which separate the trabeculæ and the Haversian canals of the cortex.

DEDUCTIONS AND CONCLUSIONS.

Having given a resume of the experiments, the details of which are to be found at the end of the paper, we may now proceed to formulate our deductions and conclusions. When we consider the first two series in which complete fractures were studied we have the condition which exactly simulates that encountered by the clinician. As mentioned previously, this is not the ideal state in which to study the activities of the individual portions of the bone, but since it is the form in which injury to the bone most frequently is met, we should have some definite ideas as to the general process.

Dupuytren has classified the process of the repair of bone into five distinct stages, based upon macroscopic findings. The periods he distinguishes are, in brief, as follows:

1. From the first to the tenth day: This is the period immediately following the fracture and is associated with the infiltration and engorgement of the tissues by blood. The resulting coagulum is absorbed between the ends of the fragments and there is a viscid, gelatinous material poured between the ends which (he says) plays an important part in the final repair of bone. The medulla becomes swollen and hardened and of a reddish, fleshy, or pulpy appearance as a result of a sort of gelatinous infiltration.

2. From the tenth to the twentieth or twenty-fifth day: In this period the callus, which is mostly cartilaginous, takes definite shape, the soft tissues becoming isolated from it. The medullary membrane obliterates the canal and proceeds to cartilage and osseous tissue formation. The whole mass constitutes the provisional callus.

3. From the twentieth to the thirtieth, fortieth, or sixtieth day, according to the rapidity of the work of reproduction, the age, constitution, and health of the patient. In this period the cartilage becomes converted into bone, the entire provisional callus becoming spongy bone. The muscles and tendons become free, but there is absolutely no union between the ends of the fragments.

4. From the fiftieth or sixtieth day to the fifth or sixth month: In this period the provisional callus becomes condensed from spongy to compact bone and the medullary canal is obliterated by osseous matter of greater or less density. The substance between the fragments is reduced to a mere line of a different color from the bone itself; it gradually assumes more consistency, loses its color, and ultimately, toward the end of the period, becomes ossified; the definite or permanent callus is then formed.

5. From the fourth or sixth to the eighth or twelfth month: During this final period the temporary callus is absorbed, the medullary cavity becomes reëstablished, the muscles and tendons perfectly free and the union is complete.

This division of the subject is very convenient and very logical when we recall that it is based upon macroscopic findings, but in the light of the present experiments it appears as if a slightly more accurate division of the process can be based upon both macroscopic and microscopic examinations. According to this method we venture to divide the process into the following periods:

1. From the time of fracture until about the fourth day may be considered the period of *infiltration*. The bone has been fractured, this being associated with free hemorrhage from the bone, medulla and all the injured soft tissues in the neighborhood. (The periosteum may also assist in the effusion of blood, but I have never found it to bleed in any operation upon a normal animal where it has been cut with a knife.) The cortex of the bone is usually fragmented, the fragments lying loose across the line of fracture, and some, at times, being driven into the medullary tissue. The blood which infiltrates all the tissues and is found at the site of fracture loses its corpuscular nature within forty-eight hours, and, in its stead, we find fibrin first as a loose network and then in dense masses. It is probably this which is described by Dupuytren as the gelatinous material appearing early between the ends of the fragments. All the tissues are moderately infiltrated by polymorphonuclear leukocytes. This infiltration disappears by the fourth day. Toward the end of this period the fragments do not appear to be quite as movable as at the time of fracture, this being due either to the edematous and engorged condition of the surrounding tissues or to the masses of fibrin between the ends of the fragments gluing them together. After the second day there is beginning cellular proliferation of the medulla and of the deeper layers of the periosteum. There is connective hyperplasia of the medulla.

2. From the fourth to the ninth or twelfth day may be considered the period of *temporary callus formation*. During this period we see a gradual absorption of the products of hemorrhage in the soft tissues, which is replaced by a connective-tissue hyperplasia. The periosteum, which was beginning to show proliferation, now becomes very thick. Its deeper portions consist of large polygonal cells which, at some distance from the site of fracture, secrete a homogeneous matrix in lines at right angles to the cortex, which matrix becomes calcified to form osteoid trabeculæ. Some of the cells are included in this mass and become bone cells. The remainder arrange themselves as a layer upon the trabeculæ as the osteoblasts. The spaces between the trabeculæ become vascularized and medullary spaces are formed.

Nearer the site of the fracture the cells of the periosteum in many cases appear to be embedded in a homogeneous matrix, which is more hyaline in character and does not appear in streaks, but is diffuse. It shows no tendency to calcification, and is probably the earliest stage of cartilage formation.

In the medullary cavity the endosteum undergoes the same proliferation that the periosteum has displayed, with a similar formation of osteoid trabeculæ at some distance from the site of fracture. The medulla becomes hyperplastic, with a decrease of the fat cells and an increase in the connective tissue and medullary cells. Between the ends of the fragments there is usually fibrin with gradually increasing connective tissue and, in some cases, cartilage.

All the processes described increase, so that at the end of this period there is a fair amount of callus present, often, when the position is fairly good, forming a complete sheath of the fragments. The callus usually consists of osteoid tissue on both fragments, with cartilage at the line of fracture; osteoid tissue in the medullary canal, and connective-tissue or cartilage between the ends of the fragments.

3. From about the twelfth to about the eighty-fifth day may be designated the stage of *reorganization*. During this period there is augmentation of the callus where most needed and absorption in the places where callus is not required. Osteoclasts are to be found in close proximity to osteoblasts, the one causing absorption along definite lines, while the other strengthens the weakened points along the new lines. The deeper portions of the periosteal callus become channelled in a direction parallel with the old cortex, while the more superficial portions under the periosteum and along the lines of stress and strain become very dense by the action of the osteoblasts. The cartilage, which has assumed definite shape and size according to the amount of displacement of the fragments (especially angular), becomes gradually converted into osteoid trabeculæ. Ossification originally occurred throughout the mass of cartilage, but as the latter becomes more localized the conversion occurs only at the edge of the mass. The trabeculæ which are in the medullary cavity also undergo some absorption. Across the line of fracture there is no osteoid tissue, but merely dense connective tissue or, at times, cartilage. During this period the cortex suffers great absorption by osteoclasts, the widened spaces, in many cases, again being lined with osteoblasts. These spaces communicate freely with the spaces between the medullary and periosteal trabeculæ.

4. From the eighty-fifth day to the end of the longest period of any of these experiments is the stage of *permanent callus formation*. During this period there is extensive absorption of all the callus and cortex, with a reapposition of apparently much denser bone in the dilated spaces. We now notice the formation of distinct lamellæ in the trabeculæ. What is most important and the part that distinguishes this period, is the fact that osteoid tissue appears across the line of fracture. It is at first very porous and its spaces communicate with those of the cortex. This latter becomes denser until it appears even denser than the original bone. The cartilage gradually disappears, the time at which this occurs varying according to the amount present.

5. As far as I am concerned this is only theoretical, but it seems that there must be a period, as described by Dupuytren, in which, in simple fractures, there is complete absorption of all the provisional callus and a complete restoration of the medullary canal. The latter of these experiments show that there is a tendency for this to occur. This should be known as the period of *absorption*.

It will be seen from the above that the views herein expressed and those formulated by Dupuytren coincide in many respects. His idea of a provisional and a permanent callus is most heartily endorsed. In none of the experiments and in none of the cases that I have seen clinically has there ever been, as claimed by Hamilton, Gaillard, and Paget, what would appear to be direct union between the ends of the fragments without the interposition of callus. The fact that in fractures that had apparently united perfectly there is, up to about three months, nothing but cartilage and connective tissue across the line of fracture, is one that is never considered, although it may be of considerable clinical importance. Jacquemin evidently recognized the clinical importance of the fact that the callus was pliable for a considerable length of time, for he succeeded in correcting angular displacement by extension and gentle pressure several months after the apparent union of the fracture. That a condition similar to that found in these experiments occurs also in human beings is beautifully substantiated by a case encountered in one of the dispensaries of this city. The patient was a young man who had sustained a concussion of the brain and a fracture of the ulna below the olecranon. He recovered from the concussion and the fracture united completely in extension. At the end of six weeks he presented himself for the first time at the dispensary for treatment for ankylosis of the elbow-joint. There was apparently perfect union of the fragments in good position accompanied by ankylosis of the elbow-joint in extension, there being only a very limited range of motion. *X*-rays (Fig. 36) show clearly the line of fracture with the fragments in perfect position. Had the bone united by osseous tissue this line would no longer have been visible. The man was etherized and the adhesions in the elbow broken up and the arm placed in acute flexion without any injury to the fracture whatever.

The proper explanation for the appearance of cartilage in the callus appears to me extremely hard to arrive at, if at all possible. Should we consider it a reversion to the embryonal state we must naturally ask why it occurs only in the region of fracture and not throughout the periosteal and medullary callus, and why it does not appear in a single one of the sawcut experiments. If it is due to motion of the fragments alone, how can we explain its presence in the medullary cavity of a greenstick fracture? What appears

to be the most rational explanation of its appearance is that it is due to a number of factors, each with its influence, and each, at times, acting independently of the others. Probably the first and foremost factor is defective nutrition and an insufficient blood or lymph supply to carry lime salts, so that the process can proceed at once to osteoid tissue formation. Angularity of the fragments with improper fixation is the most important clinical factor, causing an increase in the inflammatory conditions surrounding the parts with consequent fibrosis, and thereby impairing nutrition. The idea expressed by Matsuoka, that it is due to the amount of pressure exerted by the bandage, appears untenable. A final theory which has suggested itself as a mere possibility is that the formation of cartilage bears some relation to the fibrin between the ends of the fragments. In several specimens the cartilage was always in close prox-

Fig. 36.—Radiogram of a fracture of a human ulna of six weeks' duration showing the line of fracture still plainly visible, although the fracture was clinically perfectly united.

inity to the fibrin, which several times almost appeared to show stages of transition into cartilage. It may be that cells derived from the periosteum penetrate the masses of cartilage and secrete a substance which causes a chemical change to occur in the fibrin, with the resulting formation of cartilage. While I doubt if this is the case, the appearances before mentioned compel the suggestion.

With reference to the influence of the soft tissues in the repair of fractures, I believe with Macewen, that it does not assist but may hinder union. The only possible assistance to union appears to me to be the infiltration and induration that occurs in the tissues which may act as a temporary splint until the formation of the temporary callus. I need not mention that most of the above findings are at variance with the older views of Bordenave, Hunter, Haller, Dethleef, and others.

Leaving the subject of complete fractures as found clinically and considering it when the conditions are ideal as to fixation, etc., we see that the process is, with comparatively few exceptions, practically identical. The subject can be divided into the same periods as in the case of the clinical fractures, but the time of the periods changes somewhat owing to changed conditions. In the first place, when the sawcut operations were performed, all hemorrhage was checked before the wound was closed and the periosteum was but little damaged, not being torn and shredded as in complete fractures ordinarily encountered. This has a marked influence upon the first and second periods. During the first period the large masses of fibrin are not to be found, but the blood retains its corpuscular form for a longer period. There is a rapid reaction upon the part of the medulla which throws out connective tissue, rapidly filling the sawcut. This tissue being mostly medullary in origin, is a fertile soil for the ingrowth of osteoid trabeculæ. In addition, it is subject to no pressure and mobility to cause it to become condensed and avascular.

The importance of all these facts is readily seen when we come to the second stage of the repair. This appears in the medulla at the usual time, but in the periosteum it is late in its development, not appearing until the tenth day. The second and third periods differ very essentially from the clinical fractures in that, instead of dense connective tissue, osteoid tissue is found in abundance between the ends of the cortex. It differs also to some extent in the late appearance of reorganization, which is mostly localized to the old cortex and the trabeculæ in the sawcut. This is readily explained by the fact that there is no need for reorganization elsewhere, there being no point of greatest stress, etc. The influence upon the callus exerted by stress and strain has been very thoroughly worked out by Wolff, and I believe these experiments go far toward proving their importance and accuracy. When, in these experiments, absorption of the medullary and periosteal trabeculæ does occur, its object appears to be mostly the reduction of the bulk of the callus, which has become excessive owing to the abundant callus in the sawcut. In the simple complete fractures probably the entire stage of reorganization is for the sole purpose of making the new bone mechanically perfect. This absorption in the new lines of the bone is shown in the deeper layers of the periosteal callus and in the cortex, etc., of several specimens (Series 2) with angular displacement, where there is rarefaction of the cortex at the site which is ultimately to carry little strain (owing to the new callus occupying its former position), and condensation of the medullary trabeculæ where the new line of the bone passes through it. Thus we see structures that are normally dense becoming absorbed and structures that are normally absorbed becoming permanent.

There is probably no better place than this to call attention to a fact concerning the formation of periosteal callus that I have noticed in almost all the experiments. Almost without exception preceding or simultaneous with the formation of periosteal osteoid trabeculæ there is superficial absorption of the cortex by osteoclasts. Hofmokl has attributed the formation of pits in other portions of the bone to proliferated bone cells having several nuclei, but I have been able to find no evidence of this occurring and believe that they are caused by osteoclasts. The origin of these osteoclasts I am unable to explain. They may be medullary in origin and have the faculty of wandering through the tissues or of being carried through the blood, or they may possibly originate in the periosteum itself. To determine whether they are carried through the blood, I had differential blood counts made of a number of patients suffering from fractures, and in none were multinuclear cells found, the only change being a lymphocytosis. The fact nevertheless remains that there is superficial absorption of the cortex preceding the deposit of trabeculæ. It may be that the function of these cells is to act upon the calcareous salts, rendering them in a soluble state, to be redeposited by the action of the osteoblasts in the vicinity. Their presence cannot be attributed to necrosis of the bone, for they were found under the portions of the periosteum, which had not been disturbed, and the bone was perfectly healthy in appearance.

The fourth stage of repair is very beautifully illustrated in these experiments. The process of the union of the ends of the cortex with the trabeculæ between them and the change in direction of the canals between the trabeculæ has already been sufficiently brought out so as not to require repetition (Fig. 19). These experiments have given a new importance to the medullary trabeculæ and medullary tissue. We have seen that all the trabeculæ in the sawcut have been medullary in origin, which fact was also noticed in the complete fractures of the clinical variety. We have seen that the medullary tissue itself assists in the formation of trabeculæ by forming a framework upon which they can develop, if, indeed, the medullary tissue itself is not capable of bone formation. These experiments demonstrate that cartilage formation must be due to some extrinsic influence, since it is not present in any of the sawcut experiments. They also demonstrate that hard and fast rules for the repair of bone cannot be laid down, owing to the varied conditions under which union takes place.

When we come to consider the other sawcut experiments in which an effort was made to isolate different portions of the bone we see that the endosteum is the most active individual portion of the bone, then the periosteum, and finally the cortex; but that every portion is capable of assisting the other portions and, if necessary, performing the whole work alone. Many years ago Hilty proved the activity of the endosteum by his experiments, by which he obtained a growth of osteoid tissue in the medullary cavity by maintaining a constant pressure on the periosteal side of the cortex and also by several other experiments somewhat similar to those performed by the writer.

The osteogenetic property of all portions of the bone has a very important clinical bearing, for it means that in operations upon bone, nothing whatever should be removed excepting what is absolutely diseased, for even loose fragments of bone, as shown clinically by Macewen and experimentally in this work, can assist in the formation of callus. The medulla has too long been held in more or less contempt and has been carelessly destroyed on many occasions when it could have been saved.

Finally, in considering the possibility of regeneration of bone after subperiosteal resection the experiments cited herein would seem to prove the claim of Ollier that complete regeneration of the bone is possible after subperiosteal resection and would tend to place the operation of Nichols upon a still firmer basis. The precaution taken by Nichols to wait until periosteal trabeculæ can be demonstrated before removing the shaft is based upon sound principle, for I have never found osteoid trabeculæ in the periosteum that has been raised from the bone and is not in contact with osseous material. Should the periosteum be removed before it has begun the formation of osteoid trabeculæ the probable result would be that found in these experiments, viz., the formation of cartilage. This would doubtless later ossify, but the process would be very slow. These experiments appear to offer two choices in cases where it would be possible to do the operation very early. In the first place a bridge of healthy bone can be left between the two ends as tried by Nichols and proved of value by these experiments, or, what appears to be still more efficacious, healthy medulla, if obtainable, can be placed between the two surfaces of the periosteum. I have not had time to experiment with the transplantation of medulla of different species between the layers of the periosteum, but if this should prove feasible a great advance in bone surgery would be achieved. The exact modus operandi of the medulla in these cases is difficult to explain excepting that it may mean the introduction of tissue that has potent osteogenetic properties, is easily vascularized, and contains many osteoclasts to obtain calcium salts from the neighboring bone. Whatever may be the cause it certainly appears to assist in the regeneration and deserves further trial and study. The importance of the presence of calcium salts suggests the placing of these in powdered form, between the layers of the periosteum.

As a final word the following conception of the bone may be ventured in an effort to render more comprehensible the claims made above. If we consider the bone in the light of an organ similar to other organs, for instance, lymph glands,

we can describe it as having a cortical and medullary portion and being surrounded by a capsule. The capsule corresponds to the fibrous layer of the periosteum. The cortex corresponds to the deeper layer of the periosteum, the endosteum, the cellular tissue in the Haversian canals, and the bone cells. The medulla consists of loose connective tissue and cells of various size and shape, exhibiting blood-forming properties. In portions it is extremely infiltrated with fat. Some of its cells are multinuclear and appear to have phagocytic properties.

With the above as a working hypothesis we can explain upon physical grounds the varied activities of the different portions of the cortex. The bone cells being within very close quarters, and separated from most stimuli by dense calcareous walls, are slow to react and can only form bone when liberated from their close confines. The periosteum has much more freedom to expand and is much more exposed to external stimuli, so that it responds more quickly. It has not, however, owing to the fibrous capsule, the freedom from pressure that the endosteum enjoys, and therefore is not quite as active as that membrane. In addition, the close proximity of the endosteum to the vascular portion of the organ gives it a richer nutrition and we have more rapid growth.

Upon the basis of this theory we may explain the presence of osteoclasts upon the superficial surface of the cortex as being periosteal in origin, since all the soft tissues of the bone are related, one to the other, and of common origin. Therefore, as the medulla is capable of forming mononuclear and multinuclear cells of different nature so also may the periosteum be capable of forming osteoblasts and osteoclasts.

SUMMARY OF CONCLUSIONS.

1. In regeneration of bone all the various elements, viz., periosteum, cortex, endosteum, and marrow, assist in the process.

2. In their activities they appear to bear more or less reciprocal relations to one another, so that the absence of one can be compensated for by the others.

3. The activities of the endosteum and the medulla can be brought into play by slight stimulus.

4. The periosteum, even when proliferated, is incapable of forming osteoid trabeculæ unless in close contact and union with previous bone formation or calcareous salts.

5. Periosteal bone formation is usually preceded by superficial absorption of the cortex through the action of osteoclasts. These possibly liberate lime salts in the tissues, for the osteoblasts to again precipitate in the surrounding hyaline matrix.

6. Cortical bone-forming activity does not manifest itself until after considerable absorption of the cortex has occurred, so that it may be due to the liberation of bone cells which take on new activity and again precipitate the liberated calcium salts in new situations; or it may be due to the opportunity for the ingrowth of endosteum into the widened spaces.

7. In unimpaired regeneration of defects of bone the defect is filled with trabeculæ and spaces that originally run at right angles to the line of the bone, but rearrangement occurs in the later stages, with a change in the directions of the canals of the new bone. This is the normal function of cortical activity.

8. The medulla assists in the formation of osteoid trabeculæ by means of a skeleton framework along which the trabeculæ form and also, possibly, by the activities of some of the marrow cells.

9. The deposit of calcium salts in certain lines to form trabeculæ is not due to bloodvessels, as the spaces between the trabeculæ, until some time after they have been formed, do not contain bloodvessels.

10. Cartilage is a pathological but constant feature of the repair of complete fractures. It is not found in normal regeneration free from extrinsic influences.

11. The formation of cartilage may have some direct or indirect relation to the masses of fibrin found in the region of the line of fracture or may represent a retarded development of osteoid tissue due to poor nutrition.

12. In complete fractures the amount of cartilage present depends mostly on the angularity of the fragments, and it is always found in a wedge shape on the internal side of the angle.

13. Complete fractures are very slow in their final union, so that in the case of vicious union they may be safely rebroken up to nine months and even longer without danger of fracturing the bone in another situation. They may even be made to yield to constant traction in the proper direction.

14. There is usually sufficient callus formed on the internal side of an angularly deformed fracture to almost reëstablish the original line of the bone from one joint to the other, but with commensurate shortening.

15. In subperiosteal fractures the repair is probably mostly from the endosteum and medulla because of the extravasation of blood into the medullary canal, injuring the medulla to a greater extent than the periosteum.

16. In repair of greenstick fractures the endosteum and medulla are probably the dominant factors.

17. Regeneration of the bone after subperiosteal resection is usually cartilaginous in nature when sufficient time has not elapsed before the operation for the formation of periosteal osteoid trabeculæ.

18. A strip of healthy bone, when left between the two fragments of the resected bone, hastens osteoid regeneration.

19. Healthy medulla, when sutured between the apposed

surfaces of the periosteum, hastens considerably the regeneration of bone.

20. The process of the repair of complete fractures may be divided into the following five stages:

1. Infiltration.
2. Temporary callus formation.
3. Reorganization.
4. Permanent callus formation.
5. Absorption.

21. Similar stages are probably found in the human subject also, with slight differences, owing to the size and nature of the species.

22. The deeper layer of the periosteum, the endosteum, the tissues lining the Haversian canals and the bone cells are probably all related or identical tissues, exhibiting different activities because existing under different physical conditions.

23. Cartilage is converted into osteoid tissue in several different ways, depending upon the age of the cartilage and the stage of the fracture.

24. Osteoid tissue, when seen in ground section, is not as dense in structure and has a deeper yellow tinge than normal cortex, probably due to some difference in chemical composition.

25. Specimens of bone, with their soft parts attached can be ground to microscopic thinness, but they possess no advantage over decalcified specimens beyond demonstrating canaliculi.

26. Investigations of regeneration of bone, when not accompanied by microscopic study, are untrustworthy and often deceptive.

(To be continued.)

SOME IMPROVEMENTS IN THE STERILIZATION OF CULTURE MEDIA, WITH ESPECIAL REFERENCE TO THE FRACTIONAL METHOD.[1]

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(From the Pennsylvania State Department of Health Laboratory, University of Pennsylvania.)

The not infrequent occurrence in the course of bacteriological research of discrepancies of results, or even of total failure of the experiment when apparently the technical procedures were faultless, coupled with apparently inexplicable contaminations in culture or in a medium after storage for a time, have led the writer to suspect the methods of primary sterilization in vogue as lacking uniform sufficiency and induced the following study of this subject:

In a medium which had been sterilized in the autoclave at 15 to 20-pounds pressure for from fifteen minutes to one-half hour, and thereafter kept at room temperature and examined daily, it was sometimes observed that in the course of a few days a growth had occurred in some of the tubes, and only in exceptional instances were the tubes all free from contamination after a period of from three to six months. In case of nutrient gelatin, sterilized at 10-pounds pressure for ten to fifteen minutes, no instance was observed during the period of this study in which all of the tubes remained permanently sterile; and in one lot, after maintenance of the tubes for one to two weeks at 37° C., over one-half were found contaminated. Similar results were obtained with culture media sterilized by the fractional method, as usually recommended (heating on three successive days at 100° C. for thirty minutes, with the media left at room temperature in the intervals). With such faults in mind it was deemed desirable to make a close study of the causes of these irregularities and to attempt some modification of procedure promising greater certainty of complete sterilization.

Satisfied from comparative examinations that the fault is one entering from incompleteness of primary sterilization, it at once suggested itself that an important proportion may be due to the presence of spores resistant to the ordinary measures to which the medium is subjected. Apparet, a century ago, was the first to discover the method of conservation of preserves in stoppered bottles after the bottles had been boiled; but in his experience, in spite of boiling the containers well for several hours, it was not an infrequent occurrence that the preserves spoiled. Globbin, in 1888, observed in case

[1] Read before the Pathological Society of Philadelphia, December 13, 1906.

of an organism isolated from potato that the spores were capable of resisting 100° C. for from five to six and one-half hours, of withstanding 109° to 113° C. for three hours, and required for destruction exposure to temperatures of 113° C. to 116° C. for twenty-five minutes, or of 130° for three minutes. In the same year Koch found the spores of B. carrotarum to resist 100° C. for eight hours, and to require four hours' exposure to 130° C. sterilization. In 1894 Flügel obtained similar results with spores of certain bacteria isolated from milk. Christ, in 1895, found spores of organisms isolated from the soil capable of resisting 130° C. for one minute. The valuable researches of Heinze, in 1903, are well known in connection with B. megatherium, B. ellembachensis, and B. subtilis, the spores of the last capable of resisting 100° C. for three hours. I was able to observe in experiments made along the same line in the Institut Pasteur the capability of the spores of B. subtilis to resist exposure for two and one-half hours to 100° C. In case of the bacteria isolated from fresh bread it is familiar knowledge that their spores have resisted the heat of the baking oven. Many similar common examples of such resistive power readily occur to mind; and literature records numerous observations of facts of the same import, indicating the possibility of the dependence of failure to destroy original contamination of material by such heat-resisting entities.

It must be quite probable, too, that in addition to the above possible fault the protection afforded to contaminating organisms against the sterilization exposure may contribute in no unimportant measure to the same end. While the B. tuberculosis and the other non-spore-bearing organisms are easily destroyed by a direct exposure to 60° C. for from ten to fifteen minutes they are capable when protected by albumenoid substances (sputum, feces, etc.) of resisting for long time an exposure of 100° C. While in Berlin the writer had the opportunity of observing in the case of the tubercle bacillus, the retention of virulence by organisms obtained in scrapings from the walls of one of the tuberculosis wards after the room had been empty for over four months. Explicable in the same principle, it is a well-known fact that the sterilization of bouillon or any liquid medium is more easily accomplished than of agar or more especially nutrient gelatin; in fact, the writer has observed the complete sterilization of bouillon after a single exposure of thirty minutes to 100° C., but has never obtained similar results with gelatin.

Although the above factors (special resistance of contaminating spores and the protection afforded contaminations by the medium) might well explain imperfections of sterilization by the autoclave, it suggested itself that in case of fractional sterilization (in which as is known the spores are permitted to germinate in the intervals of heating and in their vegetative form become susceptible of destruction by the subsequent heat exposures) this failure might find another explanation, and with this in view the following investigation was pursued.

Nutrient gelatin was distributed in tubes previously sterilized by dry heat at 180° to 200° C. for fifteen minutes or longer (until a browning of the cotton plug appeared, which indicated the decomposition of the organic matter or complete sterilization) and sterilized by fractional or intermittent exposure to 100° C. for fifteen to thirty minutes on three successive days, being left at room temperature during the intervals; but in spite of all precaution taken, in a number of these tubes, after storage at room temperature or in the incubator at 37° C. in the course of from twenty-four hours to several days' contamination became apparent, the varying time apparently being related to the temperature of storage locality. This last at once suggested that in case of contamination by spores resistant to heat the room temperature exposure of the intervals might very well not be the most favorable temperature for germination of such spores in the vegetative forms; in other words, the spores present originally and not destroyed by the exposure to 100° C. in the first might at the temperature of the interval remain as such (unchanged) and be equally resistant to the heat of the sterilizing process on the second day, and that the same results might follow for the second interval and on the third heating, and that subsequently during the prolonged storage of the medium they might germinate. An experiment made in this line proved such to be the case.

Old cultures of Bacillus subtilis and spore-bearing moulds were inoculated in different media and left at room temperature, daily observation showing the medium to remain perfectly clear for from one to seven days, according to the temperature of the room and season of the year. These two organisms were preferred because, in the writer's experience, these have been found the most common and in many cases the sole agents of medium contamination. This variation in rapidity of development suggested that in the process the room temperature intervals might prevent the germination of spores, as this might well be deficient, and that, therefore, it must be desirable to provide in these intervals of sterilization surroundings of a temperature more favorable for the spores to germinate and cause the vegetative stage of growth. With this in view gelatin medium, after the first exposure to 100° C. for thirty minutes, was tubed—the tubes divided into groups. Part were placed in the incubator at 37° C. for six hours, other series were incubated at the same temperature for twelve, eighteen, and twenty-four hours, respectively; after such periods resterilization at 100° C. for thirty minutes was again performed for each group and the tubes stood at 37° C. for observation. As was expected, but few tubes subsequently were found contaminated, the results being much more favorable than when the room temperature had been employed in the intervals of

heating. Further, it was noted that the short interval of incubation, for but six hours, was too short for germination of the spores even at body temperature; and that on the other hand, eighteen to twenty hours' incubation was too protracted, since in these periods the medium became undesirably clouded for growth of the organisms, while intervals of incubation for from twelve to eighteen hours gave the most favorable results. Following these determinations another series of observations were made for the purpose of comparisons between the common practice of heating three times in fractional sterilization and two exposures. A series of tubes were heated for thirty minutes to 100° C., then incubated at 37° C. for from twelve to eighteen hours and submitted to a final sterilization at 100° C. for thirty minutes. A second series of tubes were exposed on three successive days for thirty minutes at 100° C. and incubated at 37° C. for twelve hours in the first interval, and for twenty hours in the second interval. The results in these two series were practically identical, both being satisfactory.

With a view of determining the possibility of completing a fractional sterilization in a single day, as in case of need of some media for which the use of the autoclave is unsuited, as a sugar or gelatin medium (the high temperature of the autoclave producing undesirable changes in such media), a medium was prepared early in the morning and sterilized at 100° C. as usual at about eight o'clock, then incubated at 37° C. until about five o'clock in the evening, when it was again sterilized as previously. The results were quite satisfactory, again proving the efficiency of the method and establishing the advantage of material saving of time. Such procedure can, however, be recommended only for use in emergencies, as the writer feels the need of strongly emphasizing the desirability of incubating any medium for at least forty-eight hours after sterilization is supposed to be complete, in order to detect and then eliminate any possible contamination.

It is deemed unnecessary to recommend or outline any special rule for the above procedures. Good results may be obtained by the usual practice of sterilizing on three successive days, with a first interval of twelve hours for incubation and a second interval of twenty-four hours; or by sterilizing but twice, with an interval of twelve hours for incubation; and as just stated, the sterilization can be completed in a single day. The routine method followed by the writer, with most satisfactory results, includes the preparation of the medium early in the morning and at once exposing it to 100° C. for about ten or fifteen minutes, then incubating at 37° C. for six to eight hours during the same day, and toward evening again subjecting it to 100° C. for fifteen to twenty minutes, followed by a second interval of incubation at 37° C. over night, and a final heating the next morning to 100° C. for thirty minutes. This shortens the general routine by one full day, and, too, the heat exposure is reduced by one-third, each a material advantage when at the same time the final result is not impaired, but, as above indicated, rendered more sure of success. The precise method may vary with the judgment of each worker, the writer's only desire being to point out the necessity for providing a temperature during the intervals of heating which will favor the germination of the spores, so that in their vegetative form they may be the more certainly destroyed at the next period of heating, and at the same time to urge the fact that the ordinary room temperature cannot by any means be regarded as favorable for this purpose in the intervals commonly allowed between sterilizations.

There is a further feature bearing upon the above which it is not inappropriate to bring forward in this relation. In spite of all precautions ordinarily taken in sterilizing media either in the autoclave or by the above outlined fractional method the writer has not found it always possible to avoid contamination of some of his tubes. It must be recalled that by either method the cotton plugs become more or less wet from exposure to the steam atmosphere and from the vapor arising from the heated liquid medium; and it is to be expected that by mere capillarity a more or less continuous thin sheet of the condensed moisture will intervene between the plug and the glass of the container (present in the cotton plug as well, but, perhaps, not in as perfect continuity). Through such a continuous liquid it is possible that occasionally organisms coming from the air of the open room in which the tube is cooling might be afforded a path of entry from the exterior to the interior of the tube; and it must be realized that the lower the room temperature when the tube is first brought from the heated sterilizer the more decided a current of air is drawn through the plug, as the interior air becomes cool and contracts, possibly aiding in the introduction of organisms, as just suggested. To avoid such a possibility the transference of the medium from the sterilizer to an incubation oven at 37° C. for at least forty-eight hours most clearly aid, drying the surface of the plug more quickly and at the same time permitting, to a less degree, the rarefied air in the tube to cool and condense rapidly. Personally, the writer is inclined to believe that lack of this precaution is not infrequently responsible for the contaminations which enter to spoil this or that experiment, to cause contradictory results in the work of the same or different investigators, and which have added much to the uncertainties and volumes of our bacteriological literature.

Some may be disposed to hold that if the medium has been properly sterilized, subsequent incubation for forty-eight hours, as above suggested, at 37° C. is unnecessary. This is in theory true, but in practice what means do we possess of knowing surely whether the medium is pure, save by subjecting it to conditions known to be most favorable

for growth of contamination, if perchance contamination exists? The time is past when water analysis was limited to its physical properties alone; and just as today no one would pretend to estimate the number of bacteria in a sparkling water or its sanitary condition by its clearness in the same way, we are not justified in assuming that because a sample of bouillon or other medium remains transparent after storage at room temperature or in the refrigerator, as usually recommended, under conditions unfavorable for the germination of spores possibly present, it is, therefore, a sterile medium. The procedure recommended is logically correct and so simple that no objections of inconvenience or lack of necessity should be held material against it; and it may be urged as a definite rule of procedure that in all sterilization by steam, whether in the intervals or after the fractional method, or after the use of the autoclave, the medium should not be directly exposed to room temperature or a lower temperature, but should be placed in the incubator at 37° C. because this condition will both aid in early and certain detection of possible contamination, and will in some measure favor the exclusion of organisms liable to be drawn into the container by air suction in undue moisture of the cotton plug.

The writer might add, in conclusion, that it is his opinion that the fractional method of sterilization, as above recommended, might often with advantage replace the autoclave not only in efficiency of sterilization, but more especially as evading the production of undesirable changes which the high pressure and temperature of the autoclave have been found to produce in culture media.

It is with pleasure that I desire to express my appreciation and sincere thanks to Dr. Allen J. Smith, Professor of Pathology at the University of Pennsylvania, for his valuable criticisms on this paper.

BOOK REVIEWS.

Diseases of Children. By Geo. M. Tuttle, M.D. Edited by Bern B. Gallaudet. Philadelphia and New York: Lea Brothers & Co., 1906.

For the student of medicine the condensation of a large subject such as Pediatrics into a volumn of pocket size may be of legitimate value, but the subject usually suffers so much in the process of being reduced to didactic statements that the attempt seems hardly justified by the result. In this volumn the author has covered the study of Pediatrics in as comprehensive a manner as the limits of the binding will permit, and in the main has succeeded in giving the essentials of symptomatology, diagnosis, and treatment. In etiology and pathology and in the enumeration of atypical but frequently encountered forms of disease, much could be desired, although hardly more could be expected. The grouping of the diseases follows an orderly system, but exception may be taken to placing acute rheumatism among the disorders of nutrition and cretinism among the diseases of the nervous system. While the feeding of infants is discussed at length it would seem that the method of preparing and feeding buttermilk deserves some mention as well as the subject of fat-indigestion. In the chapter on cardiac diseases not sufficient attention is paid to the so-called functional murmurs nor to the myocardial changes which probably play so large a part in the cases of disappearance of mitral regurgitant murmurs. An attempt to differentiate the protean forms of essential diseases of the blood has wisely been omitted, but the simplification has been carried too far when simple anemia and chlorosis are classed as synonymous and when splenic anemia and lymphatic anemia included with Hodgkin's disease under the title of pseudoleukemia. The differentiation of acute diffuse nephritis from acute parenchymatous nephritis, mainly by the fact that the former leaves behind a damaged kidney after the acute attack, is a distinction without a difference, or at least one that is recognizable by any methods which can be applied in vivo. Into the domain of treatment the critic fears to tread, but the use of antimony as an emetic in laryngeal diphtheria and of the finger nail in opening a retropharyngeal abscess or in dividing an adhesion of the tongue will hardly receive general recommendation. Omissions from the category of diseases are not numerous, but those of neurasthenia and of the status lymphaticus, particularly in reference to sudden death in infants, are noteworthy.

On the whole, therefore, the book is a condensed but comprehensive treatise on Pediatrics from which the student can obtain much useful knowledge, but which can be considered only as a preparatory course to the study of a more elaborate exposition of the subject.

J. C. G.

Essentials of Obstetrics. By Charles Jewett, A.M., M.D., Sc.D., Professor of Obstetrics and Gynecology in the Long Island College Hospital, etc. Third edition, revised and enlarged. Pp. 413, with thirty illustrations and five colored plates. New York and Philadelphia: Lea Brothers & Co., 1907.

The name of the distinguished author of this well-known little book carries with it a guarantee of the authentic character of its contents, and a close scrutiny of the work fails to elicit any striking defect, while much that merits special mention and commendation may be noted. The book is, as its name indicates, an excellent resume of the essentials of the obstetric art, presented in a clear and concise manner. Because of the special limitation of the work we fail to note an expression of the author's preference in many of the mooted questions. Dr. Jewett's opinions upon these matters would lend an individuality to the work which would be appreciated by the reader and would be of distinct value. Among the many good things must especially be commended the full description given of the various methods up to date of fetal palpation and the positive enunciation of recognized methods of treatment of pregnancy, labor, and their complications. The section on embryology is truly excellent. A few omissions must be noted which we trust will be corrected in a succeeding edition of the book. Thus, we find no mention at all of accouchement forcé, at least under that term, although the various methods employed are described more or less fully, with the exception of the Bossi dilator, which is dismissed with a mere mention of the instrument. The dangers attendant upon the use of this dilator are not noted, and it would be interesting to know the author's views or to the value of an instrument about which so much adverse literature has appeared. We also regret to find no criticism, favorable or otherwise, of the operation of hebotomy, of which he reports 158 cases to date, with 8 deaths. This gives a maternal mortality of over 5 per cent., which contrasts unfavorably

with the results of Cesarean section in the hands of obstetric surgeons of equal ability. Cocainization of the spinal cord is not noted. In one sense this is a good feature, since Bier's method, we think, should be mentioned only to be condemned. These are all points of minor import, however, and while a consideration of their individual merits would add to the value of the book, their omission does not materially detract from the many good things that find a place in a work which is truly excellent for its size.

W. A. N. D.

UNIVERSITY OF PENNSYLVANIA

DEPARTMENT OF MEDICINE

FOUNDED IN 1765

This Medical School, the oldest in the United States, was founded in 1765 by Dr. John Morgan, who filled in it the first medical professorship created in America. In his opening "Discourse upon the Institution of Medical Schools in America," delivered in the College of Philadelphia May 30, 1765, Dr. Morgan uttered these prophetic words: "Perhaps this medical institution, the first of its kind in America, though small in its beginning, may receive a constant increase of strength, and annually exert new vigor. It may collect a number of young persons, of more than ordinary abilities, and so improve their knowledge as to spread its reputation to distant parts. By sending these abroad duly qualified, or by exciting an emulation amongst men of parts and literature, it may give birth to other useful institutions of a similar nature, or occasional rise, by its example, to numerous societies of different kinds, calculated to spread the light of knowledge through the whole American continent, wherever inhabited."

Through Dr. Morgan, the pupil of Hunter in London and of Cullen in Edinburgh, the graduates of this school take a just pride in regarding it as the lineal descendant of the best medical schools of Great Britain in the last century. To Dr. Morgan was soon joined another pupil of Cullen, Dr. William Shippen, as Professor of Anatomy and Surgery, thus forming another tie of relationship to the celebrated University of Edinburgh, whose methods of instruction were substantially adopted here. In the next year Dr. Adam Kuhn was added as Professor of Botany and Materia Medica; and in June, 1768, a "Commencement was held," at which medical honors were bestowed, the first in point of time in America. In 1769, Dr. Benjamin Rush was elected Professor of Chemistry, while Dr. Thomas Bond, one of the trustees of the College of Philadelphia, delivered lectures on Clinical Medicine in the Pennsylvania Hospital.

To the faculty thus composed of Morgan, Shippen, Bond, Kuhn, and Rush, have succeeded, at various times, professors whose reputation has been national, such as Wistar, Barton, Physick, Chapman, Hare, Gibson Horner, Dewees, Jackson, George B. Wood, Hodge, James B. Rogers, Carson, R. E. Rogers, Leidy, Henry H. Smith, Pepper, Francis Gurney Smith, Stillé, D. Hayes Agnew, Goodell, W. Pepper, Jr., and Ashhurst.

ADMISSION.

Admission to the Department of Medicine may be obtained either: I, by diploma; or II, by examination; or in certain cases, as specified below under I, by a combination of both methods.

I. Admission by Diploma: Any candidate who may have received a degree in Arts or Science from a college recognized by this University will be admitted without examination. Candidates who may have been admitted by examination to the two-year course in Biology of this University, and who may have satisfactorily completed the course, will be exempt from the entrance examination. Any candidate who may present written evidence of having passed the entrance examinations of a recognized college, in which the requirements are equivalent to those demanded for entrance to the Freshman Class of the College (Arts and Science Courses) of this University, will be admitted without examination.

Diplomas of public high schools may be accepted as complete or partial certificates. All diplomas presented by candidates will be referred to Faculty Committee No. 1 of the College Faculty (Academic), who will examine each case and decide whether the diplomas shall be accepted in lieu of examinations, and what subjects they properly cover. The diploma must be transmitted to the Dean of the Medical Faculty not later than June 10 or September 10 in each year, and must be accompanied by a certificate signed by the principal of the school, stating the exact amount of each subject covered by the diploma, and the mark or grade attained in each subject.

II. Admission by Examination: The required subjects of examination for entrance to the Department of Medicine are the same as those prescribed for admission to the Freshman Class of the College (Arts and Science Courses) of the University of Pennsylvania.

The course of instruction extends over four years, with one session, beginning the last Friday in September and ending on the third Wednesday in June in each year.

James Tyson, M.D., Professor of Medicine.

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Edward T. Reichert, M.D., Professor of Physiology.

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John Marshall, M.D., Nat.Sc.D., LL.D., Professor of Chemistry and Toxicology.

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Alexander C. Abbott, M.D., Pepper Professor of Hygiene and Bacteriology.

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UNIVERSITY OF PENNSYLVANIA MEDICAL BULLETIN.

SURGICAL CONDITIONS ARISING FROM THE BRANCHIAL CLEFTS, WITH REPORT OF A CASE OF BRANCHIOGENIC CARCINOMA.

By John Speese, M.D.,
Assistant Instructor in Surgery, University of Pennsylvania.

(From the Laboratory of Surgical Pathology, University of Pennsylvania.)

The cervical tissues and those structures in the immediate vicinity, because of their complicated embryological development, become commonly the seat of certain congenital defects. Thus we have, for example, those errors of development due to non-union of the branchial clefts, resulting in branchial fistulas and cysts; cysts and fistulas springing from remains of the thyroglossal tract, and the so-called mixed tumors of the salivary glands originating from misplaced fetal structures. It is the intention of the author to deal with the first of these complications at present, and to consider the others in a future contribution.

Embryology. According to Semi's[1] description, about the end of the first month of fetal life, the pharyngeal cavity is formed, lying under the frontal process and bounded on the sides by four plates. These plates form the four branchial arches, three clefts remaining between them which, in early life, unite with the exception of the second. From this one is formed the cavity of the tympanum, the Eustachian tube, and the external auditory canal. The neck in this manner is developed from continuous lateral walls. The origin, then, of branchial fistulas or cysts must correspond to one of these branchial clefts, and it has been demonstrated clinically that the second and third are most commonly the origin of the defect. Their relationship to surrounding parts is of great importance, for they are usually intimately associated with the large vessels and lie near the pharynx and larynx—facts which become of surgical importance in their radical removal.

Fistula. It is now generally admitted that lateral fistulas originate from the second branchial cleft, whereas those situated in the median portion of the neck arise from the thyroglossal duct. The external opening, in complete fistula, is located in various positions between the hyoid bone above and the sternum below, the sternomastoid muscle and the midline on either side. The opening is usually quite small, admitting only a probe of the finest calibre. The internal opening of the fistula is in the region of the tonsil and terminates in the lateral wall of the pharynx. In its course it pierces the subcutaneous tissue and fascia, runs parallel with the sternomastoid on the deep fascia above the sternohyoid and sternothyroid muscles to the great wing of the hyoid bone, over the internal carotid and between it and the external, and finally under the digastric to the pharynx. The fistulas are lined with epithelium, which, if originating from the internal portion of the branchial cleft, is cylindrical, and contains large amounts of lymphoid tissue in the wall, proving its entodermic origin. The external lining is squamous, arises from ectoderm, and does not contain lymphoid tissue. The wall is composed of concentric layers of connective tissue.

The fistula, which may be complete or incomplete, is usually unilateral, and occurs most commonly on the right side of the neck. At times it is palpable as a cord-like structure beneath the skin, and not infrequently causes an annoying eczema by the constant discharge of its secretion. The diagnosis can be easily made by the injection of colored fluids, or by those which can be tasted by the patient after their injection and passage to the pharynx through the fistulous tract.

The diagnosis having been made, the question of treatment arises. Many cases are cured by radical operation, a measure however, which is formidable and should be practised by only the most skilful operator. At times the tract cannot be completely removed because of the dense adhesions and its intimate relationship with important structures. Such a case was seen recently on the service of Dr. Frazier, two previous operations having been attempted, both proving ineffectual, and followed by a return of the mucoid discharge. A third attempt was no more successful on account of the dense cicatricial tissue completely hiding the fistula, and when seen some months after the operation there was a profuse discharge from the external opening.

Operation is not always indicated, for in some cases the dangers of such procedures are obviously greater than from the existence of a small fistula producing few symptoms. The following case illustrates this fact: Surgical Dispensary, No. 6333, M. S., female, aged seventeen years. At the age of three months the mother of the patient noticed a swelling below the angle of the jaw on the right side, which later opened and discharged a thin, watery fluid. This discharge has persisted until the present, is more profuse after eating, but does not cause any discomfort or any inflammatory reaction

of the skin. The opening was so small that a probe could be introduced only with great difficulty. Operation was not advised because of the practical absence of symptoms, although in cases of this type, or in those refusing the more radical measures, the injection of corrosive fluids and the use of electricity has effected cure in some instances.

Branchial Cysts. These have been defined by Senn as cystic tumors of the neck originating from congenital defects of development, their matrix being composed of fetal epiblastic or hypoblastic tissues which remain in the embryonal state for an indefinite time and later, by proliferation of their epithelial elements, give rise to a distinct and characteristic type of cystic tumor.

The cysts are at times congenital; as a rule, however, they develop about the time of puberty and appear as oval, elastic tumors which are fluctuating. They have in general the same boundaries as the fistula, although the largest ones may occupy a considerable portion of the neck, when they produce pressure symptoms. Histologically, the same characteristics, as seen in the branchial fistulas, are present, the products of the epithelial lining being accountable for the cyst contents. Depending upon the nature of the contents, the cysts have been classified as mucous, atheromatous, serous, and hemato-cysts. They are apt to be confused with strumous conditions, cold abscesses, aneurysm, and dermoid cysts.

Branchial cysts may persist entirely as a local manifestation, producing disturbance only by pressure. Mention should be made, however, of the fact that suppuration of the cyst at times occurs, producing a so-called branchiogenic abscess—a condition which is of interest both from the diagnostic standpoint and from the malignant degeneration which such abscesses tend at times to incite.

T. B., aged forty-three years, noticed, by accident, a swelling in the right side of the neck four months before admission. The swelling steadily increased in size, was somewhat tender on pressure, and occasionally caused slight difficulty or discomfort in swallowing. There was no dyspnea, fever, or loss of weight. On examination, the mass extended from the ear and the angle of the jaw downward, and was about the size of an orange, the skin not discolored, and freely movable. The mass was firm but not hard ill-defined, did not fluctuate, and was firmly connected with the surrounding tissues. The regional lymph nodes were not enlarged. At the operation by Dr. Frazier, the sternomastoid was divided, the tumor mass being adherent to it and to the large bloodvessels. The growth was completely removed, was opened and found to contain pus, when for the first time the possibility of a branchial cyst was suspected, the symptoms and findings suggesting a sarcomatous formation. Microscopically, the wall of the cyst was the seat of an inflammatory process, contained much lymphoid tissue, and here and there showed an epithelial lining not destroyed by the inflammation. The lining consisted of squamous cells which, with the presence of lymphoid tissue, made the diagnosis of a branchial cyst apparent. The wound healed by first intention and the patient was discharged as cured.

Branchiogenic Carcinoma. The primary development of carcinoma of the neck was first observed by Langenbeck,[1] although the true nature and origin of such growths were described by Volkmann, who named them branchiogenic carcinoma. Since the publication of Volkmann's[2] cases, there have been several notable papers written on the subject, the majority of which confirm his belief as to the derivation of the growths; some writers, however, take exception to his views.

The origin and development of branchial defects resulting in benign conditions have been alluded to. In general the views are uniform, but considerable diversity of opinion exists as to the source of primary carcinoma of the neck, other than those whose origin is obvious. During the formation of the branchial arches and clefts, islands of epithelial tissue become displaced and may remain latent for years in the cervical tissues without producing symptoms. Under the action of certain unknown irritants, however, they proliferate and give rise to primary carcinoma. On the other hand, we have branchial cysts undergoing a malignant degeneration of its epithelial lining, and in the literature we can find numerous cases which confirm this view. The history of a cystic formation which may have existed for years without producing any noteworthy symptoms, is often obtained. Without apparent cause there may arise a sudden increase in size of the cyst, and on further examination evidences of cancerous transformation are evident. A case observed in Bruns'[7] clinic proves almost conclusively that a branchial cyst undergoes carcinomatous change. The patient had a branchial cyst which, having persisted for years, underwent suppuration and was drained. A year after the operation the remaining portion of the sac began to grow rapidly, and an examination of the same revealed a squamous carcinoma. The case to be reported by the writer closely resembles the above one. Gutmann[8] has endeavored to trace the origin of these tumors to aberrant thyroids rather than to misplaced epithelium of branchial origin. His opposition to the teaching of Volkmann, however, has not been sustained entirely by histological, embryonic, or clinical knowledge. Gussenbauer[10] holds another view, for he observed in certain cases that the lymph nodes situated along the internal jugular vein were absent, and that lymphoid tissue, or even whole nodes, were at times included in the cyst wall. For these reasons he believes that it is possible for such carcinoma to spring from lymphoid tissue, and in some instances he thought a direct transition of lymphoid

cells into epithelium arose. Perez[11] doubts the view of Gussenbauer, although he thinks that epithelium is found in lymph nodes, and that such a primary origin of neck cancers is possible. If the metaplastic origin is not accepted, the epithelial cells must have been transported in some manner to the lymph nodes, there to multiply and form a primary lymph-node carcinoma. Perez believes these cells are derivatives of the branchial clefts, and therefore these tumors are in reality of branchiogenic origin and can be classified with those which result from the degeneration of branchial cysts or fistulas. The transportation of epithelium through the lymph stream to the axillary nodes and the formation of primary carcinoma there have been observed. In spite of the fact that such growths are of branchiogenic derivation, the name of "branchiogenic carcinoma" should not be applied to them, but reserved for those tumors which are found in their characteristic location, the upper triangle of the neck, and the term "primary lymph-node carcinoma" given to the remaining types.

Having determined, then, that the tumor is of epithelial origin, we must endeavor to prove that it is with certainty a primary growth, and that it has no connection with other tumor formations. The cervical lymphatics are commonly the seat of metastatic deposits from malignant tumors which are situated on the face, in the mouth and its neighboring cavities, the tongue, salivary and thyroid glands, the pharynx, larynx, esophagus, and even the stomach. It can thus be seen that the primary origin of a secondary tumor of the neck could escape observation, although, as a rule, only those situated in the stomach or esophagus should give rise to any diagnostic difficulty. The primary esophageal cancers are situated in the lower third, and frequently produce dysphagia and other symptoms suggestive of stenosis. In any case the esophagoscope should make the diagnosis clear. That the diagnosis is not always easy or possible is shown by a case operated upon by Jordan, in which a supposed primary neck cancer was removed. The autopsy disclosed a small carcinoma of the esophagus, which had not narrowed its lumen, the metastasis of which had closely simulated a branchiogenic growth, the mistake emphasizing the caution which should be used in diagnosis, and especially in radical treatment. A recent case occurring in the service of Dr. Stengel (*Surgical Pathology*, No. 1267) showed a metastatic growth in the cervical region, a mass the size of an egg being located in the lower triangle. Here the symptoms pointed to an esophageal lesion and such a growth, situated directly at the cardia, had given rise to a secondary squamous carcinoma, the metastasis occurring about one year after the primary symptoms of an esophageal lesion had begun, the symptoms being indicative of a malignant stenosis.

Symptoms. The disease occurs practically always in males, the age varying from forty to sixty-five years. The typical location is limited above by the ramus of the lower jaw, below by the level of the lower border of the thyroid cartilage, behind by the sternomastoid, and in front by the median line of the neck. In this position the tumor may begin, at first showing but little tendency toward a rapid growth, but sooner or later it increases rapidly in size and may involve a large portion of the neck, exceeding the boundaries mentioned. As it breaks through its capsule and infiltrates surrounding parts, the cancer becomes adherent to these structures, and necessitates the removal of the sternomastoid muscle and other important tissues during operation. The subjective symptoms now become marked; the pain is severe and often radiates to the ear or occipital region. It may be constant or spasmodic in character. The surface of the growth is hard and indurated, although there may be areas of softening, such necrotic points having a tendency toward perforation of the overlying skin. As the process advances, disturbances in swallowing and respiration develop, due in part to direct pressure, or to compression and involvement of the nerves. The patients die from complications or cachexia, which, in this form of malignancy, is early and rapid, the patients dying in six to eight months. Metastasis is rare, occurring in only 4 of the 36 cases collected by Brunet.[9]

Diagnosis. The diagnosis, as has been stated, is difficult, and in some cases may be corroborated only by the positive or negative findings of a postmortem examination. The characteristic location of a painful tumor, rapid growth, adherence to the surrounding parts, the history of a cyst, and, if possible, the exclusion of a growth elsewhere, may reveal the nature of the tumor. Secondary growths in the lymphatic nodes do not develop so acutely, are painless in the beginning, do not exhibit the early and rapid tendency to infiltrate, and cause adhesions to surrounding parts. The diagnosis of other affections, such as actinomycosis, tuberculosis, and lymphosarcoma can readily be made by the excision and examination of a portion of the growth. The prognosis is grave and the percentage of deaths high, operation in only 3 cases having been followed by freedom from recurrence. Eigenbrodt's[7] case lived two years, 1 of Brunet's one year, and the case reported three years without showing signs of further involvement. As a rule recurrence appears in three to five months after operation, and is soon fatal. The prognosis is also unfavorable because the frequent division of the vagus, occurring four times in twenty operations, predisposes to pneumonia. The prognosis could be greatly improved if operation were resorted to earlier, at a time when the growth was still contained within its capsule, and had not infiltrated the soft parts of the neck. The majority of the cases treated have all been advanced ones, involving the large vessels and demanding an extensive and radical dissection. The operation in several of the early cases has been

easy, and it has been observed in these instances that complete extirpation of the growth with its capsule can be accomplished.

Treatment. The advantages to be derived from an early operation have been discussed. From a prophylactic view, it seems rational to remove when possible branchial cysts and fistulas, in order to prevent the malignant, and not so uncommon, carcinomatous degeneration. The results of the operation depend upon laying the site of involvement freely open, and for this reason, Shimanck[6] recommends the flaps and cross-cuts of Bruns and Gussenbauer. The first incision is parallel with the sternomastoid; the second runs from the middle of the chin obliquely to the middle of the sternomastoid, and then to the acromion process of the scapula. The muscle is divided and, if diseased, resected, and the flaps turned back. It is frequently necessary to ligate the internal jugular vein, the carotids less often. Since the vessels have undergone more or less gradual compression, and the blood supply of the brain is largely assured by the vessels of the opposite side, the ligation of these compressed vessels does not produce the serious complications which are likely under other conditions. Division of the vagus if infiltrated by tumor tissue is not so dangerous as might be supposed, its regulating action being assumed by the compensatory power of the opposite or sound vagus.

The author wishes to thank Dr. John B. Deaver for permission to report the following case of branchiogenic carcinoma, and Dr. Charles H. Frazier for the case of branchial abscess already alluded to:

H. F. Y., aged thirty-six years, male. The family and personal history of the patient do not reveal anything which has any connection with his branchial lesion. Three years before his admission to the German Hospital he noticed a swelling on the right side of the neck; there was an entire absence of pain, but the growth did interfere somewhat with the movements of the neck. On examination the mass was found to be fluctuating and movable to a slight degree because of adhesions to surrounding parts; the skin was not involved in any respect. The case was diagnosticated as an abscess, which was opened and drained, a portion of the abscess wall being removed for microscopic examination. The latter revealed a connective-tissue framework which contained a considerable amount of lymphoid tissue and a lining of stratified epithelium. The bloodvessels were greatly dilated, presumably as the result of the abscess formation. Extending from the epithelial lining downward into the lymphoid and connective tissues below, there was an infiltration of the flat squamous cells. This epitheliomatous formation was not extensive, and did not form pearly bodies. The diagnosis of malignancy arising in a branchial cyst having been made, a radical removal of the sac was determined upon and the operation performed by Dr. Deaver. As the process had not extended deeply into the wall of the cyst, complete removal of the latter was not difficult, few adhesions being encountered.

Three years from the date of the above operation the patient is entirely well and does not show any signs of a recurrence.

Aside from the pathological rarity of this case, it is of interest also because of the similarity it bears to Bruns' case of branchiogenic carcinoma, which, likewise, developed from the irritation of a preëxisting branchial abscess. The early recognition of the lesion, the microscopic examination at the time of the first operation, and the radical removal of the tumor mass immediately when its nature was known, all contributed to the success of the operation, an extension of the carcinoma into the deeper tissues thus being prevented. The age of the patient, thirty-seven years, is unusual, the majority of the cases reported being about sixty years of age. The period of three years without any tendency toward recurrence is also worthy of comment, for, while few of these cases have recovered, none have been free from a secondary involvement for this period of time.

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A CASE OF MIXED-CELL LEUKEMIA.

By Wm. W. Cadbury, M.D., and Wm. T. Cummins, M.D.

(From the Pathological Laboratory of the University of Pennsylvania.)

A review of the literature on leukemia which has appeared in the last two or three years indicates that the main points under discussion at the present time may be classified under five headings, as follows:

1. What is the ultimate etiological factor in the production of the leukemias?

2. The histogenesis of the abnormal cells circulating in the blood and the primary seat of the process.

3. A proper classification of the different varieties of the disease.

4. The influence of intercurrent infections.

5. The beneficial results obtained by the use of the *x*-rays.

Considering first the ultimate cause of the disease we must frankly admit that there is no definite knowledge. The theory of a parasitic origin has recently been reviewed by Auer.[1] In a typical case of leukemia with a leukocyte count of 135,000, 95.78 per cent. of which were large lymphocytes, rounded, refractile bodies of various shapes and sizes were found in some of the larger cells. These objects resembled in some ways the Leishman-Donovan bodies. Another theory is advanced by Hoffmann,[2] who reports 4 cases treated favorably with the Röntgen rays. He endeavors to explain the improvement on the basis of a new theory of the disease process. Thus, if we assume that the hyperplasia of the bone-marrow and myeloid degeneration of the spleen are vicarious or compensatory processes caused by a chemotactic irritation of the blood, then any alteration of the blood through the action of the rays removes all occasion for hyperplasia of either the leukocytes or even the marrow and spleen; wherefore, the cells are reduced in number and the spleen becomes smaller.

Another theory of the nature of leukemia, which has many adherents at the present time, is that which considers it a neoplastic process allied to sarcomatosis. This view is upheld by Banti.[3] Warthin[4] calls the process in general a leucoblastoma, which he subdivides into a non-chloromatous and a chloromatous variety. The first includes the more common forms of leukemia as well as lymphosarcoma, pseudoleukemia, etc. Warthin[5] in support of this theory also contributes a case beginning as Hodgkin's disease and later developing the typical blood picture of a small-celled lymphatic leukemia with postmortem findings closely resembling those of Hodgkin's disease. The most recent contribution to this phase of the problem is given by Banti[6] in the *International Clinics*. The author here states that the changes affecting the bloodvessels may be classified under four groups, viz.: (1) Hyperemia, (2) hematopoietic, (3) nodular lymphadenoid, (4) diffuse lymphadenoid. The tissue is not hyperplastic, but may rightly be called neoplastic, since it is of a typical structure and tends to invade neighboring tissues. Moreover, it gives rise to metastases. Banti goes on to describe myelogenous leukemia as a systemic myeloid sarcomatosis of the hemo- and lympho-poietic organs. Myelocytes are neoplastic cells which enter the circulation after rupture of a metastatic area into the blood stream.

This neoplasm theory is denied, however, by Ménetrier and Aubertin, who suggest that there may be a simultaneous proliferation of several types of cells equally differentiated and reproducing a normal myeloid tissue indicating a diffuse hyperplasia of the hematopoietic system rather than a neoplasm. Grawitz[7] further combats the theory, stating that the sarcomatosis idea is completely overthrown by the fact that leukemic infiltrations never show a tendency to spread to adjacent organs. Moreover, the lymphatic structures may be wholly unaffected. Both of these factors throw much doubt on the sarcomatous nature of the process. Again, *x*-ray treatment, which is markedly beneficial in leukemia, is usually valueless or even harmful in cases of sarcoma.

The old division of the leukemias into lymphatic and splenomedullary is undergoing considerable change. In fact, Grawitz states that the only proper division is into acute and chronic. In general, the acute forms are characterized by a uniformity of cells, while the chronic usually show a variety of types, but that this is not an invariable rule is shown by the occurrence of very acute forms in which many myelocytes are found. Mager and Sternberg[8] cite a case of this kind in which the patient died on the twenty-seventh day. There was marked splenic enlargement but a normal proportion of leukocytes three days before death. At the postmortem, however, all the appearances of a myeloid leukemia were present and the blood of the corpse showed about 21 per cent. of neutrophilic myelocytes.

As to the proper differentiation of the various pathological types of the disease, two main theories have been formulated. The first, according to Neumann, Walz, and Pappenheim, would define all varieties of leukemia as manifestations of a single pathological process, invariably produced by an abnormal condition in the bone-marrow. The variations in the manifestations of the disease are caused by the fact that in some instances the myeloid elements of the marrow are chiefly affected; in other cases the lymphoid elements are the seat of the morbid process.

The other theory as formulated by Ehrlich sharply differentiates lymphatic from myelogenous leukemia. The former is due to a primary proliferation of all the lymphadenoid tissues, including also a portion of the marrow. The myeloid type of leukemia, on the other hand, is a result of affection of the marrow alone. Thus myeloid leukemia is an active leukocytosis. In lymphatic leukemia we find a passive dissemination of cells in the blood derived from the enlarged glands. The question of pathology rests largely on how we shall dispose of the medium-sized lymphocytes which arise both from lymphatic and marrow tissue.

Hirschfeld[9] considers that no case should be called mixed leukemia except where one finds a typical myelemic blood picture with a very high percentage of lymphocytes, including especially the larger variety. At the same time one should be able to find numerous glandular enlargements showing histologically active proliferation of large lymphocytes. However, no sharp line of demarcation can be drawn. Moreover, he considers it improbable that the leukemic process originates in the blood stream. Browning[10] reports a case of mixed-cell leukemia and concludes that such a blood picture may be caused (*a*) by a reversion of myeloid cells to the embryonic, non-glandular type, or (*b*) a reaction or mechanical disturbance of the myeloid tissue may take place as a result of the lymphoid hyperplasia, with the passage of myelocytes into the circulation. He also considers that under certain conditions lymphoid and myeloid tissue may be concomitantly affected in a manner similar to that which occurs in a simple myeloid or a simple lymphoid leukemia. In such a case a mixed leukemia might be said to exist in the strict sense of the word.

This subject is admirably summarized by Grawitz as follows, in his *Klinische Pathologie des Blutes*, p. 428:

1. In every case of leukemia there must be a pathological proliferation of the white marrow cells, with dissemination of these cells in a state of immature development into the blood.

2. As a rule every variety of cell is found in the blood, *i. e.*, mononuclear neutrophiles, basophiles, and eosinophiles; mononuclear cells without granules, but with basophilic homogeneous protoplasm; transitional forms from the non-granular to the granular types, and finally very large and delicate mononuclear cells.

3. In a small number of cases the homogeneous mononuclear cells of various sizes appear out of all proportion to the other varieties.

4. When spleen and lymph glands are affected an uncertain number of mononuclear cells may be derived from these organs.

In connection with our own case the result of an intercurrent infection is of interest, especially tuberculosis. Many instances of simple or septic infection have been cited in which there was a temporary fall in the leukocytic count, with diminution in the size of the spleen. For example Lichtheims[11] reports a case in which with the development of tuberculosis the leukocytes fell from 250,000 to 8900, while the polynuclear percentage rose from 50 to 90. Similar cases are reported by Parker,[12] Elsner,[13] Jungers,[14] Weil,[15] Stintzing,[16] Beitzke,[17] and Murrell.[18] Funck[19] reports an instance of general infection due to a pyonephrosis which was greatly relieved by appropriate treatment. During the height of the infective process the number of leukocytes fell rapidly, but when the source of the infection was removed the leukocytes returned to their previous number. With the onset of the infection the spleen decreased in size, as also the superficial and bronchial lymphatics. These organs were filled with myeloid proliferations or metastases of leukocytes produced in the bone-marrow. With the infective process the polynuclear cells made their way into the blood with consequent diminution in the size of the spleen and lymph glands which failed to retain this type of cell. A similar improvement in the blood count with a diminution in the size of the spleen has resulted from the injection of tuberculin.

After considering the more important features of our own case it will be evident that it should be classed among the chronic leukemias, for though symptoms of œdema and enlarged lymph glands extended over a period apparently not greater than six months, yet, with the history of progressive weakness lasting for two years and the chronic course of the disease while under observation, the process was certainly not of the acute variety, thus conforming with Grawitz's statement that mixed-cell leukemias are usually chronic. As to the influence of the tuberculous process in the lung it appears to have been quite without influence on the course of the disease, either in reducing the size of the spleen and lymph glands or in altering the blood picture. This may doubtless be explained by the fact that the tuberculous process was an exceedingly chronic one and no signs of active disease were observed in the affected lung.

The report of the case is as follows:

N. R., male, white, aged fifty-six years. Occupation, farmer. He was admitted to the medical wards of St. Mary's Hospital, September 7, 1906. The clinical notes are given by permission of Dr. M. H. Fussell, under whose care the patient remained until he left the hospital.

Family History. Mother died of dropsy and a brother of bronchitis; otherwise no important facts bearing on the case were obtained.

Previous Personal History. Ten years ago patient was much run down and suffered with a very bad cough. He gradually became much better, but developed pneumonia a few years ago, and for the last two years has often suffered with very bad colds.

Present Illness. For the past few months the patient has been steadily growing weaker. Since June, 1906, he has

noted a marked edema of the hands and feet. For three months he has been very hoarse. During the summer of 1906 he was seen by a physician, who told him he had an enlarged spleen. Little change in the condition was noted during the patient's stay in the hospital. The *x*-ray treatment was not employed. Fowler's solution was administered in ascending doses. After remaining in the hospital about one month he returned to his home in the country, on October 12, 1906. The details of the further progress of the disease were not ascertained except that the patient became progressively weaker and the dropsy increased. Death occurred November 17, 1906.

Physical examinations were made from time to time by Dr. Fussell and others during the patient's stay in the hospital, with the following results:

The skin is of a lemon-yellow color, though the pallor is not that of an anemia. The left arm, forearm, and hand are very edematous. The right arm is scarcely swollen at all. Both legs are edematous. The abdomen is distended and there is marked anasarca of the belly walls and external genitalia. The chest is relatively small. The supraclavicular glands, especially on the left side, are greatly enlarged. The superficial lymphatic glands are everywhere palpable and most of them are decidedly enlarged.

Heart: Area of dulness apparently normal. The sounds are feeble, with a faint systolic murmur at the base.

Dr. J. T. Ulom noted an area of dulness with many crepitant rales over the upper portion of the right lung.

The spleen is greatly enlarged, extending from a point about on a level with the seventh rib to two inches below the umbilicus.

Laryngoscopic examination showed slight swelling of the epiglottis.

Temperature: The temperature rose to 99° twice, but during the greater part of the patient's stay in the hospital, however, it did not rise above 96°. The pulse averaged 80 beats to the minute and the respirations averaged about 24. One examination of the urine was made, showing a specific gravity of 1016. No albumin, glucose, nor casts were found.

Blood: The blood was examined on six occasions:

September 20, 1906. Leukocytes, 156,000. First smear stained with hematoxylon and eosin: Polymorphonuclear neutrophiles, 62.3 per cent.; small mononuclear lymphocytes, 12.6 per cent.; large mononuclear lymphocytes, 6.4 per cent.; eosinophilic polymorphonuclears, none; transitional cells, none; neutrophilic myelocytes, 17.8 per cent.; basophiles, none.

Second smear of same date, stained with Wright's stain: Polymorphonuclear neutrophiles, 52.6 per cent.; small mononuclear lymphocytes, 19.8 per cent.; large mononuclear lymphocytes, 3.3 per cent.; eosinophilic polymorphonuclears, 3.1 per cent.; transitional cells, 1 per cent.; neutrophilic myelocytes, 11.5 per cent.; basophiles, 8.4 per cent. No nucleated erythrocytes are found.

29*th*. Erythrocytes, 2,876,000; leukocytes, 170,000.

October 3, 1906. Erythrocytes, 3,000,000; hemoglobin, 50 per cent.; leukocytes, 250,000. Differential count of 1500 leukocytes: Polymorphonuclear neutrophiles, 47 per cent.; small mononuclear lymphocytes, 20.4 per cent.; large mononuclear lymphocytes, 7.1 per cent.; eosinophilic polymorphonuclears, 1.1 per cent.; transitionals, 6.7 per cent.; basophiles, 1 per cent.; neutrophilic myelocytes, 16 per cent. A few normoblasts, microblasts, and megaloblasts are seen.

8*th*. Leukocytes, 260,000.

9*th*. Leukocytes, 248,000; hemoglobin, 60 per cent. Differential count of 1100 leukocytes: Polymorphonuclear neutrophiles, 48.5 per cent.; small mononuclear lymphocytes, 17.4 per cent.; large mononuclear lymphocytes, 5.6 per cent.; eosinophilic polymorphonuclears, 3.1 per cent.; transitionals, 3 per cent.; basophiles, 3.3 per cent.; neutrophilic myelocytes, 18.4 per cent.; eosinophilic myelocytes, 1 per cent. A few normoblasts and microblasts are seen.

11*th*. Leukocytes, 210,000. Differential count of 300 leukocytes: Polymorphonuclear neutrophiles, 53 per cent.; small mononuclear lymphocytes, 16.6 per cent.; large mononuclear lymphocytes, 7.6 per cent.; eosinophilic polymorphonuclears, 1 per cent.; transitionals, 2 per cent.; basophiles, 2 per cent.; neutrophilic myelocytes, 17.3 per cent.; eosinophilic myelocytes, 0.3 per cent.

The autopsy was performed in the house of the patient, on November 18, 1906, at 4 P.M., about seventeen hours after death, with the assistance of Dr. J. T. Ulom and Mr. Karl Smith.

General Appearance. The body is that of a man of average size, apparently well nourished. Rigor mortis present. Some lividity of the dependent portions of the body. Very marked edema of all the subcutaneous tissues, especially the feet, external genitalia, and face. There is very marked pallor of the skin and mucous membranes. The superficial lymphatics can all be readily palpated and many are so enlarged as to form visible tumors, *e. g.*, in the groins, above the clavicles, etc.

Abdominal Cavity. On making the median incision the subcutaneous fat of the anterior abdominal wall is found to be almost absent and there is marked edema of the subcutaneous connective tissue. The peritoneal cavity contains a large quantity of clear amber fluid. The serous surfaces are for the most part smooth and free from adhesions, except in the hypochondriac and epigastric regions, where the liver, spleen, intestines, and anterior abdominal wall are firmly bound together by fibrous adhesions. The appendix is apparently normal.

Thoracic Cavity. On opening the thorax the lungs do not collapse. The sternum appears normal. The cut ends

of the ribs appear swollen and yellow marrow exudes from the cancellous spaces.

The right pleural cavity is completely obliterated by very firm fibrous adhesions, which in many places cut like cartilage. The left pleural cavity is free from adhesions. The serous surfaces are smooth and glistening and the cavity contains a considerable quantity of clear amber fluid. The *right lung* shows a few caseous areas at the apex. The whole organ is traversed by extremely dense fibrous bands, between which are found cicatrized caseous lesions appearing like old tubercles. The lung is nowhere crepitant. The *left lung* is more voluminous than the right. It is everywhere crepitant and of a mottled gray color. On section no cicatrices are to be seen; a small amount of frothy fluid exudes from the cut surfaces, which on close examination shows innumerable light points—the dilated alveoli.

Pericardial cavity contains a slight excess of clear, straw-colored fluid. The surfaces are smooth and glistening.

The *heart* is enlarged, especially to the right. There is a large milk spot on the anterior surface. The myocardium is dark red in color and its consistency slightly decreased. The leaflets of all the valves are thin, delicate, and apparently normal, except one of the aortic leaflets, which shows some thickening. The ascending portion of the arch of the aorta is smooth. The right ventricle is dilated. Yellowish bands are observed beneath the epicardium, probably leukemic infiltrations. The *mediastinal and bronchial lymph glands* show very marked enlargement, some of them reaching the size of an English walnut.

The *spleen* is enormously enlarged, exceeding the size of the normal liver and weighing 2050 grams. It is firmly bound to the adjacent structures by fibrous adhesions. The external surface is rough on account of old fibrous tags and is of a pale slate or pink color. The cut surface is of a rather light purplish color.

It is shining, smooth, and moist, very closely resembling the cross-section of a normal liver. The hyperplasia of the pulp far exceeds that of the trabeculæ.

The *liver* is slightly enlarged and very firm in consistency. On section the cut surface is smooth and of a *café au lait* appearance.

The *left kidney's* capsule strips readily. Both the external surface and the surface of the cut section show numerous yellowish areas of lymphoid hyperplasia. The cortex is narrower than normal.

The *right kidney* offers the same picture as the left, only to a less marked degree.

The *ureters* and *bladder* are apparently normal.

The *right adrenal* is apparently normal.

The *intestines* show no marked gross lesions. The mesenteric lymph nodes and the peritoneal and retroperitoneal lymphatics are everywhere greatly hypertrophied. A few hemolymph glands are seen in the peritoneal cavity.

Anatomical Summary. Hydroperitoneum and chronic adhesive peritonitis; hydrothorax, chronic obliterative pleuritis, chronic fibroid and caseous tuberculosis and emphysema of the lungs; hydropericardium, leukemic infiltration of the subepicardial tissue, right ventricular dilatation and chronic aortic valvulitis; chronic splenic tumor; leukemic infiltration of the kidneys; hyperplasia of the lymph glands and bone-marrow.

Histological study was made of the following tissues: (1) lungs; (2) heart; (3) liver; (4) spleen; (5) pancreas; (6) kidney; (7) adrenal; (8) small intestine; (9) lymph glands; (10) bone-marrow.

1. (*a*) *Left Lung.* Pleura is absent. The feature is the distention and rupture of many of the air vesicles. The emphysema is of moderate grade. In a few scattered areas there is noted an infiltration of the alveolar walls with lymphocytes and polymorphonuclear leukocytes which has caused considerable reduction in size of the air vesicles. The arteries are engorged with practically equal parts of erythrocytes and leukocytes, a condition which is found in all the congested organs. There is no fibrosis nor arteriosclerosis present. A moderate amount of carbon pigment is present in its usual distribution.

(*b*) *Right Lung.* Pleura is absent. The feature is the great increase of connective tissue. In many places the tissue has been replaced by rather dense masses of fibrillated connective tissue with but little of the vesicular structure remaining. Considerable of the fibrillated tissue has undergone a hyaline metamorphosis, while certain well-defined areas present an appearance of mucous tissue. One large area contains an infiltrate of lymphocytes and eosinophiles. What little vesicular structure remains is for the most part emphysematous. The squamous epithelium which normally lines the alveoli shows a reversion to the columnar type. Not a little of this has desquamated.

(*c*) *Right Lung.* One large, well-defined area contains numerous fibroblasts and young bloodvessels. There are a few corpora amylacea present in the air vesicles. Otherwise the tissue is similar to (*b*). There is no evidence of tubercles in (*a*), (*b*), or (*c*). (Tubercle bacilli were demonstrated in the tissue, however.)

2. *Heart.* The epicardium shows nothing abnormal. The feature is the dense infiltration of the subepicardial tissue with leukocytes, especially of the lymphocytic type. There are a few polymorphonuclear leukocytes present. Section of the coronary artery and vein are included in this area and the infiltrate is especially dense in the immediate vicinity of the latter structure (Fig. 1). There is a rupture of a portion of the venous wall. About one-third of the wall shows an infiltration of lymphocytes with considerable reduc-

tion of the fibrous and muscular tissue. The infiltrate is seen extending a short distance into the myocardium. Nothing remains of the adipose tissue except a few small vacuoles. The muscle cells are greatly atrophied, with their nuclei indistinct and cross-striations absent. Polar pigment is present in markedly increased quantities. There is a moderate congestion present. Fibrosis and arteriosclerosis are absent. The endocardium is normal.

3. *Liver* (Fig. 2). The capsule is considerably thickened with fibrous tissue. The feature is the infiltration of the

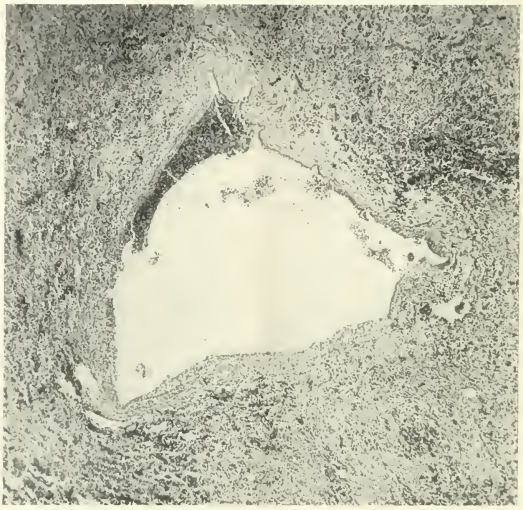

Fig. 1

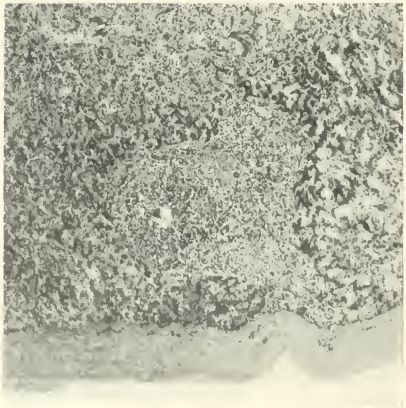

Fig. 2

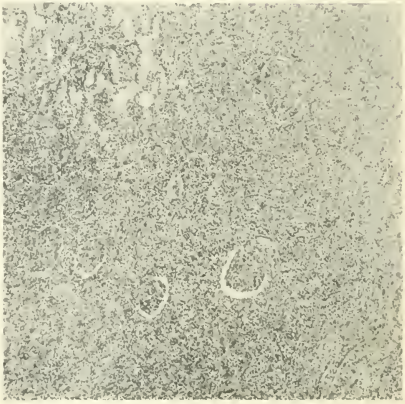

Fig. 3

entire tissue, including the interlobular areas and the lobular capillaries with lymphocytes, polymorphonuclear leukocytes, and eosinophiles. This is somewhat more pronounced in the interlobular areas. Dense masses of the cells are seen in these locations. In a few such areas the portal vein and hepatic artery have been obliterated and the bile ducts alone remain. The eosinophiles are so numerous that they may be seen with the low power. The central lobular vessels are distended with blood cells consisting of practically equal parts of leukocytes and erythrocytes. The lobular capillaries are distended with the above-mentioned leukocytes and erythrocytes. The hepatic cells are much reduced in size, and present rather faintly stained nuclei. Some fatty degeneration is seen, together with a moderate quantity of bile pigment. There is no increase of interlobular fibrous tissue.

4. *Spleen.* The capsule is moderately thickened with fibrous tissue. The trabeculæ are not increased. The Malpighian bodies are vaguely evident. There is a diffuse lymphoid hyperplasia present. Eosinophiles are seen in large numbers, together with a few polymorphonuclear neutrophiles. Numerous karyokinetic figures are seen.

5. *Pancreas.* There is a marked increase of connective tissue both in the peri- and intra-lobular areas. Some of this is hyaline in appearance. (Gentian violet and iodine green were employed, but they showed an absence of amyloid material.) There is an infiltration of lymphocytes in the perilobular areas. A large part of the parenchyma is necrotic, with the islands of Langerhans indistinct. The epithelium of the ducts shows considerable desquamation.

6. *Kidney.* The capsule is absent. Invading a considerable portion of the cortex there is a dense infiltration of leukocytes (Fig. 3). These are mostly of the lymphocytic type, but numerous polymorphonuclear neutrophilic and eosinophilic cells are present. There is widespread necrosis of the tubular epithelium, much of which remains as debris in the lumina. The Malpighian bodies are not abnormal. A moderate grade of congestion is present. The medullary epithelium is in places necrotic. Some congestion is present.

7. *Adrenal.* Here and there small areas of hemorrhage and necrosis may be seen. The pigment of the zona reticularis is present in liberal quantities. In the medulla there is a small infiltration of lymphocytes and eosinophiles.

8. *Small Intestines.* The entire mucosa is necrotic. A lymph nodule is seen in the submucosa showing a diffuse hyperplasia of its lymphoid elements. Numerous long, rod-shaped microörganisms are seen lying between the cells. There is well-marked congestion of the submucosa.

9. *Lymph Nodes.* (Five specimens.) All show a diffuse lymphoid hyperplasia. The bronchial node is considerably congested and a moderate amount of carbon pigment is seen. One of the nodes contains numerous long, rod-shaped microörganisms similar to those noted in 8). They are absent in the bronchial lymph nodes. Throughout these tissues there are numerous coarsely granular bodies which take the stain rather deeply. Their nature is as yet undetermined.

10. *Bone-marrow.* The tissue is rather loosely packed with polymorphonuclear neutrophiles and eosinophiles, nucleated erythrocytes, and the characteristic marrow cells.

Histological Summary. Fibrosis of the lung, with emphysema, congestion, and hyaline degeneration; leukocytic infiltration of the subepicardial tissue, with brown atrophy of the heart; chronic perihepatitis with passive congestion, leukocytic infiltration, bile pigmentation, and fatty degeneration of the liver; chronic perisplenitis with lymphoid hyperplasia, eosinophilic infiltration and karyokinesis; chronic interstitial pancreatitis with necrosis, leukocytic infiltration and hyaline degeneration; leukocytic infiltration of the cortex of the kidney with necrosis and diffuse congestion; hemorrhage and necrosis of the adrenal with leukocytic infiltration; congestion of the intestine with lymphoid hyperplasia; lymphoid hyperplasia and congestion of the lymph glands.

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REGENERATION OF BONE.

An Essay, Illustrated by Photographs and Photomicrographs, Dealing with the Repair of Simple Fractures and the Regeneration of Bone after Partial Injury and Subperiosteal Resection.

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(From the Laboratory of Surgical Pathology of the University of Pennsylvania.)

(Continued from page 138.)

EXPERIMENTS IN DETAIL.

All the experments were performed under the influence of an anesthetic administered usually by Mr. James Timlin. For the sake of brevity, owing to the length of the experiments, the mode of operating will not be repeated under each operation; therefore one will answer for the particular series, merely the results of the others being given.

SERIES 1.

As stated in the body of the paper, this series was performed upon rabbits and consisted of complete fractures of the foreleg, made by grasping the limb between the fingers and breaking it subcutaneously and then placing it in cotton and a sodium silicate bandage.

Experiment 1. Operation performed May 25, 1905. Animal killed May 26, 1905. Fracture of one day's duration.

Macroscopic Description. The bones were found to have been broken through completely, the end of one of the fragments projecting through the deep fascia. There was a great amount of edema of the soft tissues and some hemorrhage into the muscular tissue. The leg was embedded in the manner described under Technique, and then cut and stained with hematoxylin and eosin, which were the stains used throughout all the experiments.

Microscopic Description. Under low power the sections show an almost transverse fracture, with marked displacement and fragmentation of both bones of the foreleg. The muscular tissue in the immediate neighborhood of the fracture is markedly torn and mingled with fragments of bone. In places, portions of muscles are caught between the ends of the fragments. There is very little free blood present, but between the fragments there appears to be a loose network of fibrin. In the medullary cavity there is practically no reaction. The periosteum is infiltrated in places.

Under high power, the fibrin, muscles, detritus, and all the tissues in the neighborhood of the fracture, are seen to be moderately infiltrated with leukocytes. The specimen illustrates very well the natural union of the two bones laterally by cartilage with the absence of periosteum.

Experiment 2. Operation performed August 7, 1905. Animal killed August 9, 1905. Fracture of two days' duration.

Macroscopic Description. There was no preternatural mobility, so that at least one of the fractures must have been greenstick. On removing the skin there was found slight ecchymosis over the middle of the foreleg at the probable site of the fracture.

Microscopic Description. The fracture was complete at least in one bone, although the bones are in perfect position. The only explanation that seems to offer itself for the perfect position is that one bone may have had only a greenstick fracture. If the apparently complete fracture was greenstick, there must have been only a very slight bridge of bone left, which may have been missed in the selection of specimens for study. That this is probably the explanation is evidenced by the fact that one specimen presents the medulla not broken across, so that there could not have been much displacement.

Under low power the muscles attached to the bone are seen to be infiltrated with blood in the interspaces between the fasciculi, but there is very little injury or fragmentation of the muscles. Much of the blood maintains its corpuscular shape, but in places, between the fasciculi, there is a delicate network of fibrin formed. There is very little inflammatory reaction in the form of leukocytes, but there are some young fibroblasts. Between the fragments and extending along the line of fracture are masses of fibrin intermingled with deeply staining, red, granular masses of debris. There is slight fragmentation of the fractured ends of the bone. In the periosteum, especially in some of the sections, can be noted signs of beginning thickening, there being three or four superimposed layers of long, spindle-shaped cells, with large, oval nuclei.

The hemorrhage in the medullary cavity appears to have run up the side, separating the medulla from the cortex more than tearing up the medulla itself. In some of the

sections there are signs of proliferation of the endosteum, especially of the superficial layers, with the formation of fibroblasts or a loose connective tissue. In other sections there is marked proliferation of the deeper layers of the endosteum, with the formation of large, polygonal cells. The marrow is hyperplastic, with a change from the yellow to the red variety.

Experiment 3. Operation performed September 11, 1905. Animal killed September 14, 1905. Fracture of three days' duration.

Macroscopic Description. On removing the skin a very extensive ecchymosis with edema of the entire foreleg was found. The bones were not united, but did not appear to move as freely as when fractured.

Microscopic Description. Sections of the leg show complete fracture of at least one of the bones, with marked fragmentation of the ends of the fragments. There was not much displacement of the ends of the bone. The muscular tissues are infiltrated with young fibroblasts separating the fasciculi, but there is very little free blood present. In the immediate neighborhood of and between the fragments there are masses of fibrin, in some places quite dense, in others forming a looser network, containing in its meshes red blood cells and some necrotic debris.

There is thickening of the periosteum at some distance from the ends of the fragments, mostly of the superficial fibrous layer, which is continuous with the processes between the fasciculi of the muscles. There is also some thickening of the endosteum, especially in some areas, with the formation, in its deeper layer, of polygonal cells of the osteoblastic type with large, oval nuclei. In the medulla also are signs of hyperplasia, with the increased formation of connective tisue and bone-marrow cells, including many eosinophiles. There is a slight decrease in the number of fat cells.

Experiment 4. Operation performed July 27, 1905. Animal died July 31, 1905. Fracture of three and one-half days' duration.

No macroscopic description recorded.

Microscopic Description. There is comminution of the fragments of both bones, with poor position. There appears to be considerable hemorrhage still in the muscular tissue, which is extensively lacerated in the region of the fratute. Between the ends of the fragments and extending across the medullary cavity are plugs of fibrin, in places quite dense and in other places in the form of a loose network which contains in its meshes what appear to be red blood cells with a few leukocytes among them.

The periosteum and endosteum appear to be slightly thickened, but the cellular characteristics are destroyed.

Experiment 5. Operation performed May 25, 1905. Animal killed May 29, 1905. Fracture of four days' duration.

Macroscopic Description. There was no union or fixation apparent after removing the dressing. There was some nodulation at the ends of the fragments, which was probably beginning callus. On removing the skin general ecchymosis was found, especially in the dependent portions of the leg and at the joints.

Microscopic Description. There is absence of blood between the muscular fasciculi, its place being taken by an abundance of young connective tissue. Between the ends of the fragments, as if gluing them together, are dense streams of fibrin in which there do not appear to be any free blood or cellular elements (Fig. 1). There are also numerous fragments of bone with some necrotic debris.

The periosteum is markedly thickened, both the superficial fibrous layer and the deep osteoblastic layer, in which are large polygonal cells with large oval or round nuclei. At some distance from the site of fracture, the protoplasm of the cells of the osteoblastic layer appears to become homogeneous and fused with that of the surrounding cells, the whole mass of homogeneous material taking a pink stain, apparently only the nuclei remaining enmeshed in the mass. On the surface of this material the osteoblasts are arranged in rows. The fusion takes place in narrow lines which appear to unite and form bridges when seen in section (Fig. 2). This tissue is osteoid tissue.

In other areas the protoplasm of the proliferated cells of the periosteum seems to be transformed into hyaline material which does not take the red stain. The cells apparently fuse, but have, as yet, no definite arrangement. They have the appearance of beginning cartilage.

In the endosteum there is very marked proliferation. The deeper layers of polygonal cells are arranged in rows on the surface of the compact bone and, in places, have undergone similar homogeneous transformation and fusion, with the formation of osteoid tissue. The new formation of bone occurs only at some distance from the site of the fracture. The medulla contains many red blood corpuscles and shows connective-tissue hyperplasia, with a decrease in the number of fat cells.

Experiment 6. Operation performed August 23, 1905. Animal killed August 28, 1905. Fracture of five days' duration.

Macroscopic Description. There was no firm union of the ends of the fragments, but there were evidences of callus formation, as the fragments seemed to be somewhat bound down.

Microscopic Description. Under lower powers no free blood but an abundance of connective tissue is seen in the muscular tissue. There is marked displacement of the fragments. The periosteum shows considerable thickening, with the formation of an abundance of osteoid trabeculæ, as far as the ends of the fragments and in the bridge across the line of fracture.

The tissue across the line of fracture is composed mostly of typical cartilage, with its deep-blue staining cell surrounded by a light halo, and then a deep-blue capsule and lighter blue hyaline ground substance. There is a decided tendency toward the formation of twin cells. The cells of the cartilage are very large and very abundant, whereas the ground substance is insignificant.

In areas a transition from cartilage into osteoid tissue can be seen. The cells apparently shrink somewhat, the ground substance becomes more abundant and stains red in spots, while the cells in the intervening areas disappear and their places are taken by an invasion of connective tissue between the trabeculæ. In the younger areas this has not occurred, but large plugs of cartilage can be seen to be surrounded by transitional trabeculæ.

There is considerable proliferation of the endosteum, with the formation of osteoid trabeculæ to the ends of the fragments. It contains no cartilage. The narrow shows connective-tissue hyperplasia. Other elements cannot be distinguished.

Experiment 7. Operation performed August 15, 1905. Animal killed August 21, 1905. Fracture of six days' duration.

Macroscopic Description. There was marked ecchymosis and edema of the lower portion of the leg. There was no firm union, but the ends of the fragments were evidently united by some material that prevented free motion of them.

Microscopic Description. There are osteoid trabeculæ on the fragments, but the most interesting portion of the specimen is the dense mass of fibrin found between the ends of the bone. On its outskirts this appears to be infiltrated by connective-tissue cells, the protoplasm or ground substance of which is of a rather reddish hue. This tissue is, in turn, in juxtaposition with cartilage. On its other side the fibrin is in close relation with a mass of cartilage, which has bands of fibrin coursing through it. The whole appearance raises the possible suggestion that cartilage, which is almost invariably found on the periosteal surface and between the fragments, could be derived from organization of the fibrin by periosteal or connective tissue or osteoblastic cells.

Experiment 8. Operation performed May 19, 1905. Animal killed May 26, 1905. Fracture of seven days' duration. This operation was only a partial fracture with bone forceps.

Macroscopic Description. There was a small nodule of callus about one-fourth inch long at the site of operation.

Microscopic Description. The sections show that a fragment of bone was left in the trough made by the forceps. There is a great abundance of young cellular connective tissue, much of which has the characteristics of granulation tissue, filling in the defect of the bone, in the medullary cavity and outside of the bone. There are dense strands of fibrin at the edges of the bone wound.

On the periosteal surface, at some distance from the bone injury, there are some osteoid trabeculæ, but they are not present in such abundance as in the medullary cavity. The endosteum shows considerable proliferation. Opposite to, and lining the inside of the medullary cavity at some distance from, the bone injury, there are bridges of osteoid trabeculæ which do not extend to the edge of the wound. The osteoblasts which line the trabeculæ appear smaller than usual. Their nuclei are smaller and more deeply stained than is usually the case, and there appears to be more protoplasm. Their arrangement is not quite identical with those in simple transverse fractures.

There seems to be no effort at absorption of the loose fragments, as there are no phagocytes present, but, instead, osteoblasts surround them as if they would be used as a framework for the formation of new bone. The medulla is largely replaced by young connective and granulation tissue. The bone defect is filled entirely with granulation tissue, there being no osteoid trabeculæ present.

Experiment 9. Operation performed August 7, 1905. Animal killed August 15, 1905. Fracture of eight days' duration.

Macroscopic Description. In bandaging the leg the foot had been left out and became the seat of moist gangrene, with sloughing. This did not extend underneath the dressing. There was no callus present. The fracture was found to have been greenstick.

Microscopic Description. The fracture of one of the bones is greenstick and the other complete transverse, with no displacement of the fragments. There is practically no infiltration of the muscles with exudate or connective tissue, and no evidence of fibrin in clot except in a couple of places between the ends of the fragments.

The periosteum is decidedly thickened for some distance on both sides of the line of fracture. Under it are osteoid trabeculæ in the form of a spindle with the thickest portion opposite to the line of fracture. There is less callus present in the greenstick fracture than in the complete one. Opposite to the line of fracture is found cartilage in the process of formation and in the stage of transition into osteoid tissue. In places the cartilage cells are extremely large and in close proximity to the small remnants of fibrin remaining between the ends of the bone (Fig. 3). Cartilage is found nowhere except opposite to the line of fracture. Most of the cartilage cells take a brownish stain and the ground substance blue.

The endosteum exhibits marked proliferation and more osteoid tissue than the periosteum. The osteoid tissue in the medullary cavity also assumes a spindle shape with the thickest portion opposite to the line of fracture. That there could never have been much displacement is shown by the fact that there is a narrow strip of medulla between the two medullary spindles on the two sides of the medullary

cavity, as seen in section. There is also in the medullary canal, opposite the line of fracture, a very clear deposit of cartilage in the completely fractured bone and a minute deposit in the medullary cavity of the bone with a greenstick fracture at the point where there had been the greatest amount of separation. A fragment of bone lying loose in the medullary cavity is assisting in the formation of callus, having on its surface osteoid trabeculæ and cartilage.

The medulla is hyperplastic, there being much tissue which is myxomatous in appearance, numerous marrow cells, and a few fat cells. Between the fragments there is nothing but a small amount of fibrin, and, in places, a little connective tissue, the fragments being literally held in place by the two osteoid splints.

Experiment 10. Operation performed August 26, 1905. Animal killed September 4, 1905. Fracture of nine days' duration.

Macroscopic Description. There was a small amount of callus present and the ends of the bone were bound together, but there was some rocking motion of the distal ends of the fragments owing to the weakness of the callus. There was no mobility between the ends of the bone.

Microscopic Description. There is not a great amount of displacement of the ends of the fragments, but there is no union whatever between the apposed surfaces of the cortex. There appears to be a space between which is filled with detritus and some fibrin at the sides. The fragments are held in place by a very large amount of fibrocartilage, which extends from one fragment to the other, entirely enclosing the space before mentioned. In places this cartilage blends directly with the filaments of fibrin lining the cavity. In these situations it appears as if cells invaded the fibrin, which was then broken up into strands which were undergoing hyaline change. This is merely suggestive, and not convincing in appearance.

On the periosteal aspect of the fragments there is an abundance of osteoid trabeculæ covered by very large osteoblasts. The spaces between the trabeculæ take varying directions, but mostly obliquely from the site of fracture or almost parallel with the old cortex. The cartilage is present mostly at the site of fracture, forming a large, bulging mass at that area. Here it shows stages of transition into trabeculæ and fibrous tissue. The cells are very large and the ground substance between them becomes more prominent and takes a deeper eosin staining until gradually it encroaches on the cells and trabeculæ are formed.

In the medullary cavity there is a moderate amount of osteoid trabeculæ formation. It does not completely fill the canal, but goes up along the sides in contact with the cortex. The medulla has a hyperplastic increase of the connective tissue, with a decrease in the number of fat cells. Above this area the marrow is red and contains an abundance of very large cells, apparently with single, very large nuclei and an abundance of protoplasm. The cortex shows little or no absorption. Osteoid trabeculæ are seen forming on the surface of a loose fragment of bone.

Experiment 11. Operation performed May 19, 1905. Animal killed May 29, 1905. Fracture of ten days' duration.

This experiment consisted of a partial fracture with bone forceps.

Macroscopic Description. There was an organizing blood clot at the site of the operative wound. On the radius there was a nodule of callus about one-quarter of an inch long.

Microscopic Description. There is a great abundance of connective tissue all around the site of operation. On the periosteal surface there is a large amount of osteoid tissue which appears to take origin from osteoblasts and cartilage. This is found at some distance from the site of injury in the form of large, oval cells, with small, round, pale nuclei, the whole being surrounded by a wide halo and then a small amount of reddish-blue groundwork. In areas the ground substance increases, the cells decrease in size, and osteoid trabeculæ are formed. There is some fibrin and even free blood present.

The medulla is of the red variety, with a great increase in the connective tissue. In the medullary canal there is also some osteoid trabeculæ formation. The loose fragments do not show any proliferation on their surfaces, but, instead, show little pits or depressions in which are seen some large, brown cells, which do not stain well and are probably osteoclasts.

Experiment 12. Operation performed August 16, 1905. Animal killed August 28, 1905. Fracture of twelve days' duration.

Macroscopic Description. There appeared to be perfectly solid union of the fragments and there was very little callus.

Microscopic Description. There is a fair amount of osteoid callus, which is present in greater abundance on the periosteal side than on the medullary side of the bone. The callus is in the form of a spindle, tapering above and below the line of fracture. The position of the fragments is very good, there being no lateral or angular displacement, merely lengthening with consequent space between the ends of the fragments. In the periosteal callus the trabeculæ seem to be disposed in a longitudinal direction in the line of the bone so that the spaces between them run in a similar direction.

In the periosteal callus, surrounding the bone like a ring at the line of fracture, is a mass of cartilage with very large cells taking intense blue staining, with a blue, homogeneous, intercellular substance, and a condensation of the outer edge of the cells in the form of a capsule. On the edge of this mass of cartilage can be seen stages of transition into osteoid trabeculæ and what also appear to be transition stages into

medullary cells. In areas directly next to and lying on the cartilage, are large multinuclear cells with deep-brown pigment, the exact significance of which it is difficult to determine; that is, whether they are derived from the cartilage (since some of the single cartilage cells in the same region have a brownish tint and appear as if the capsule were disappearing), or they are acting as phagocytes to absorb the ground substance of the cartilage and leave the cells as medullary cells. These large polynuclear cells are abundant throughout all the medullary spaces of the callus. The periosteal osteoid trabeculæ are very thin or absent at the line of fracture, the union being by cartilage only.

There are osteoid trabeculæ in the medullary cavity also, but not in as great abundance as on the periosteal side of the bone. There is a narrow tube of hyperplastic, vascular medullary tissue between the endosteal callus of the two sides of the bone, connecting the medullary canal above and below the line of fracture. There is a small area of cartilage in the endosteal callus which is not continuous over the line of fracture with that in the periosteal callus. Between the ends of the fragments there are no osteoid trabeculæ, but dense fibrous tissue and some cartilage (Fig. 4). The trabeculæ are very vascular. The cortex shows great porosity and absorption with an abundance of osteoclasts and some osteoblasts, but little or no bone formation.

Experiment 13. Operation performed July 27, 1905. Animal killed August 9, 1905. Fracture of thirteen days' duration.

Macroscopic Description. There was considerable mobility found at the site of fracture. Apparently not much callus had been thrown out. On removing the skin which was adherent to the site of fracture, considerable ecchymosis was found.

Microscopic Description. The fragments are not in apposition, there being considerable displacement of them. There is no union apparent. On the periosteal side there is but little osteoid callus formation. That which is present is very porous in nature and apparently undergoing absorption, as there are abundant osteoclasts present in the spaces between the trabeculæ.

On the endosteal side of the cortex there are but very few osteoid trabeculæ, and they are near the ends of the fragments. Between the fragments there are some loose fragments of bone, an abundance of fibrous tissue, and some fibrocartilage. The trabeculæ do not appear to be covered with osteoblasts to the normal extent. The medulla is rather fibrous and not very vascular. The cortex shows marked absorption by osteoclasts, being quite porous in the region of the fracture, with numerous osteoclasts throughout the widened spaces.

Experiment 14. Operation performed August 31, 1905. Animal killed September 14, 1905. Fracture of fourteen days' duration.

Macroscopic Description. Union was fair, but a slight amount of mobility could be obtained.

Microscopic Description. There is great displacement of the fragments and splintering of their ends. They are bound together by a large mass of fibrocartilage and connective tissue, the ends being free in some sections and embedded in the cartilage mass in others. On the periosteal aspect of the fragments there is considerable growth of osteoid trabeculæ. The spaces between the trabeculæ are filled with an abundance of osteoblasts and also contain osteoclasts. They do not appear, as yet, to be vascularized. In the medullary cavity there is a moderate growth of osteoid trabeculæ along the sides, but not filling the entire canal. The medulla is hyperplastic to a great extent and, near the articular ends of the fragments, is red, containing large cells with large, single nuclei. Some of them appear to be dividing.

At the line of fracture there are remnants of fibrin which appear to be broken up into strands by the invasion of connective tissue, etc. There are varying amounts of fibrocartilage present in the line of fracture, showing formation of trabeculæ and the action of the phagocytes in forming the canals between them. The loose fragments of bone exhibit absorption on one surface and the formation of trabeculæ on the other. These trabeculæ are undergoing absorption. In the cortex there is moderate osteoclastic absorption. The muscular fasciculi are separated by connective tissue.

Experiment 15. Operation performed August 17, 1905. Animal killed September 4, 1905. Fracture of eighteen days' duration.

Macroscopic Description. Union perfect, there being a fair amount of callus present, and no mobility of the fragments.

Microscopic Description. There is some displacement of the fragments, which are embedded in a mass of fibrous tissue and fibrocartilage. On the periosteal aspect there is a liberal amount of osteoid trabeculæ which blends with the cartilage in the region of the fracture. Osteoclasts are found throughout the trabeculæ and in the connective tissue between the fragments. There are trabeculæ on a loose fragment. There is absorption of the cortex with a lining of osteoblasts in the widened Haversian spaces.

The medulla is hyperplastic and, near the articular ends, red, with very large cells having a single nucleus with a tendency to divide. There are some osteoid trabeculæ in the medullary cavity. Across the line of fracture are connective tissue and cartilage.

Experiment 16. Operation performed August 7, 1905. Animal killed August 28, 1905. Fracture of twenty-one days' duration.

Macroscopic Description. There was perfectly solid union and the site of the fracture could not be found. The

leg was dissected and a small, dark spot found which was probably the site of a greenstick fracture.

Microscopic Description. The specimen was most likely a greenstick fracture with perfect union, the site of fracture being recognizable by the greater thickening of the bone at one place, combined with increased vascularity and hyperplastic condition of the medulla, and the porosity of the bone at that situation.

It is almost impossible to distinguish callus from old bone, since whatever callus there has been is as dense as the original bone. In the medulla of the widened spaces of the cortex and in the medulla of the main medullary canal, where it is in contact with the bone (probably new), are a great number of polynuclear, brown-staining, pigmented cells (osteoclasts), some lying in pits or depressions. Lining the cavities are polygonal cells, probably osteoblasts. All the Haversian spaces on the side of the fracture are widened and are lined with osteoblasts. They contain bloodvessels or numerous spindle cells and some small, round, eosinophilic cells similar to bone-marrow cells. The marrow is hyperplastic and of the red variety.

Experiment 17. Operation performed July 28, 1905. Animal killed August 21, 1905. Fracture of twenty-four days' duration.

Macroscopic Description. The fracture was found to have been perfectly united. The ends were apparently not in close apposition and projected in places. There was not an excessive amount of callus.

Microscopic Description. There is a fairly abundant osteoid callus, especially in the periosteum. It is impossible to determine the extent of the endosteal callus, because, owing to the angular displacement of the fragments, the sections do not go through the specimen in the proper plane to show the condition of the medullary cavity in the region of the fracture. The osteoid trabeculæ appear to be in the stage of absorption, there being quite a few osteoclasts applied to their surfaces. They are also lined with osteoblasts on them. There do not appear to be any new layers of bone.

Between the fragments there are no osteoid trabeculæ, but dense, cellular connective tissue, with some cartilage containing lime salts in places. The union is apparently fibrous. There is extensive rarefaction of the bone, the widened Haversian spaces being covered, in areas, with large, multinuclear osteoclasts taking a brown stain. Some of the spaces contain bloodvessels and others merely a cellular connective tissue. In some there are apparently osteoblasts.

Experiment 18. Operation performed July 31, 1905. Animal killed September 4, 1905. Fracture of thirty-five days' duration.

Macroscopic Description. The fracture had united perfectly, with the formation of a very large callus. There was no mobility present.

Microscopic Description. There is a very large mass of callus, but the relations of the fragments cannot be determined because of great displacement. The callus is, for the greater part, fibrocartilage showing distinct stages of transition into osteoid tissue. There does not appear to be a great amount of absorption, as osteoclasts are not present in great numbers except in and around a couple of detached fragments. In portions of these fragments there is distinct lacunar absorption and in other areas a deposition of layers of new bone.

There are practically no signs of absorption of the cortex. The Haversian spaces are not dilated and there are no newly formed spaces. There does not appear to be a great amount of endosteal bone formation, most of the callus being periosteal in origin. There is a considerable quantity of osteoid tissue, especially in the portions of the callus at the greatest distance from the line of fracture. The marrow is red and hyperplastic, containing in areas abundant myxomatous-looking cells.

SERIES 2.

The operations of this series, performed upon dogs, consisted in making subcutaneous fractures of the tibia and fibula by forcibly bending them over the side of the table. The legs were placed in shaped wooden splints which were retained in position by a sodium-silicate dressing.

Experiment 19. Operation performed December 6, 1905. Animal died December 27, 1905. Fracture of twenty-one days' duration. The animal died apparently as the result of infection from an ulcer upon the abdomen caused by the bandage.

Macroscopic Description. There was no displacement, but some mobility of the fragments. A small amount of callus was present. The fibula appeared to be slightly thickened opposite to the site of fracture, but perfectly sound.

Longitudinal section through the bone revealed a very good apposition of the fragments, with only a small amount of space between the ends. There was very little periosteal callus present, but there was a thin layer of new white bone 2 mm. thick on the internal angle formed by the fragments, extending 15 mm. below and 10 mm. above the line of fracture. It was much thinner on the anterior surface of the bone. Directly opposite to the line of fracture there was no new bone, but cartilage. The medullary cavity was filled for 2 cm. above and 2.5 cm. below the line of fracture with young, reddish-yellow, very vascular, spongy bone, except for the distance of 5 mm. above and below the line of fracture, where it was cartilaginous in appearance. The nutrient artery penetrated the upper plug of bone. The line of fracture on the anterior aspect of the bone was filled with cartilage.

Microscopic Description. Between the ends of the bone nothing but dense fibrous tissue can be seen. In places, blood and fibrin intervene between this tissue and the bone. This dense fibrous tissue traverses the entire line of fracture across the medullary canal. On each side of the tissue there is a layer of fibrocartilage entirely across the line of fracture and in the periosteal callus. On the periosteal aspect of the bone there is a moderate proliferation of osteoid trabeculæ, more pronounced in places where there are inequalities at the site of fracture. The increased amount of trabeculæ fills in the depressions made by those inequalities. The trabeculæ are no longer covered with ostcoblasts in layers, but there is some absorption of the periosteal trabeculæ by osteoclasts. In the spaces between the trabeculæ there are loose connective tissue and thin-walled bloodvessels. There is considerable absorption of the cortex in some areas and none in others. These places contain numerous osteoclasts, but no osteoblasts. The ends of the fragments are undergoing absorption.

The medullary cavity is filled, to a considerable extent, with loose osteoid trabeculæ, which extend flush with the ends of the fragments, where they abut against fibrocartilage. The spaces between the trabeculæ are large and contain loose connective tissue, marrow cells, and leukocytes (polymorphonuclear). Almost all the spaces contain large, thin-walled bloodvessels engorged with blood. There is practically no absorption by osteoclasts. The connective tissue of the marrow is considerably increased in amount, but not the marrow cells.

Experiment 20. Operation performed July 3, 1905. Animal killed August 7, 1905. Fracture of thirty-five days' duration.

This operation was performed with a saw through an incision.

Macroscopic Description. There was a very small drop of pus in one stitch-hole. The deeper portions of the wound were not at all infected. There was a very large callus extending for about 12 mm. on each side of the bone wound, and projecting from the bone for about 12 mm. The union of the fragments was very firm.

Longitudinal section through the bone revealed the fact that the fracture had been made where the cancellous portion of the bone joins with the compact portion. There was perfect union of the fragments, the entire medullary cavity for 15 mm. being completely filled in with newly formed cancellous tissue, containing in areas (Fig. 5) small islands of cartilaginous tisue. The callus, on the outer aspect of the bone, extended from 2.5 to 3.5 cm. toward the epiphysis and, in places, was 6 mm. thick. The portions of the callus nearest the epiphyses and next to the old cortical bone had gone on to the formation of compact bone, being more compact the farther removed from the site of fracture. Just opposite the line of fracture, where the callus was thickest, it existed still in the form of cartilage. The bone union was mostly cartilaginous, showing that ossification proceeds from the point at which the periosteum and endosteum remain attached to the cortex.

Microscopic Description. There is some lateral displacement of the fragments. There is no actual bony union between the ends of the fragments, but a thin layer of very dense fibrous tissue, which is continuous, on the periosteal side of the old callus, with fibrocartilage.

Osteoid callus is present in considerable amount on the periosteal aspect of the bone, tapering from the line of fracture upward and downward on the fragments. In areas this tissue is dense and in other areas quite rarefied (that is, where it is abundant to fill in a defect caused by the displacement of the fragments, it is dense externally, between the end of one fragment and the side of the other, and rarefied in the deeper portions, where it is opposite the medullary cavity of the other fragment). Osteoclasts are abundant. Osteoblasts line the medullary and Haversian spaces.

The medullary canal contains a moderate amount of callus which is quite rarefied, especially in its centre. Osteoclasts and osteoblasts are present side by side. This is additional proof that the process of repair is only in progress and not complete. The marrow is red.

There is great absorption of the cortex, so that the ends, in places, appear as mere spicules. The Haversian spaces contain osteoclasts as well as ostcoblasts. There does not appear to be any hyaline cartilage present, and only a moderate amount of fibrocartilage. The remainder of the unossified tissue is dense and fibrous.

Experiment 24. Operation performed October 31, 1905. Animal died December 27, 1905. Fracture of fifty-seven days' duration.

Macroscopic Description. There was firm union of both bones, with a large callus about 25 mm. long by 12 mm. thick on the tibia and 18 mm. by 12 mm. on the fibula. There was angularity of the fragments anteriorly.

On longitudinal section through the bone, it was found that there was some displacement of the upper fragment forward on the lower fragment, so that the posterior side of the cortex of the upper fragment plugged the medullary cavity of the lower fragment. The angle on the posterior aspect caused by the projection forward of both fragments was completely filled in on the periosteal side, for a distance of 25 mm. on each fragment, with new bone and cartilage 10 mm. thick opposite the line of fracture and arranged as follows: Quite dense bone farthest removed from the site of fracture; then brownish, porous bone against the cortex to the line of fracture, where it was replaced by cartilage. This cartilage assumed the form of a bracket with its point toward the bone and its base outward (Fig. 6), being 15 mm.

at its longest point. On the anterior aspect of the angle, on the periosteal side, there was practically no callus excepting a small amount of new bone 7 mm. in extent filling the space formed by the projection of the upper fragment. The thickness of the callus almost reëstablished the straight line between the knee and the ankle. The medulla of the upper fragment was filled for 20 mm. and the lower for 5 mm. with white, spongy bone, beyond which was mottled red or yellow marrow. A thin layer of cartilage intervened between the ends of the fragments. The posterior aspect of the cortex of both fragments near the thick callus had a porous appearance, as if some absorption had taken place.

Microscopic Description. There is great angularity of the fragments. The microscopic findings confirm the gross findings. Abundant, rather dense osteoid tissue is found in the angle between the fragments. An apparently younger formation, with larger spaces than in the deeper portion, is seen on the surface. The general direction of the medullary spaces in the new bone is almost vertical to the cortex. There is some absorption of the deeper layers, with the formation of longitudinal canals (Fig. 8).

On the outer side of the angle there is very little osteoid bone formation and this does not extend to the ends of the fragments.

In the medulla one fragment is filled for some distance with quite compact osteoid tissue. This is where the outer side of the cortex of one fragment abuts against the medullary surface of the other fragment. In the medullary canal of the other fragment, where the inner side of the cortex of the previously mentioned fragment abuts against it, there is medullary osteoid tissue undergoing absorption, but not present in great abundance.

There is hardly any absorption of the cortex on the outer side of the bone away from the angle of displacement, while the cortex on the inner side next to the extensive callus has undergone considerable rarefaction with a lining of osteoblasts, bloodvessels etc., in its dilated spaces. At the line of fracture there is fibrocartilage all the way across, especially marked in the angle between the fragments where it widens out into a wedge shape. Between the fragments it a sumes more the character of very dense fibrous tissue than fibrocartilage. It is quite vascular in areas. One portion of the cortex shows no attachment to it whatever, but was evidently separated by a space. On the edges of the mass of cartilage there are evidences of advancing bone formation, the cartilage being penetrated by bloodvessels, osteoblasts (?), and marrow cells, accompanied by a deposition of calcium salts at the edge and the formation of new trabeculæ (Fig. 10). This process is well illustrated in the fibula, which presents phenomena similar to those described above. Most of the medulla is red and contains some osteoclasts.

Experiment 22. Operation performed December 8, 1905. Animal killed February 9, 1906. Fracture of sixty-three days' duration.

Macroscopic Description. The leg was perfectly united, only a very small, spindle-shaped callus being present. Longitudinal section (Fig. 7) through the medulla revealed perfect union of the fragments, which were in rather good position, there being only slight angular deformity forward, associated with slight forward dislocation of the lower fragment on the upper. The medullary cavity was continuous for a part of the distance. There was quite an abundant periosteal callus on the posterior side of the bone, extending upward on the cortex 22 mm. and downward on the lower fragment 15 mm., being 5 mm. thick at its thickest portion directly opposite to the line of fracture. The callus here consisted of firm white bone at the portions farthest removed from the line of fracture, so dense as to be almost indistinguishable from the old bone. As it approached to within 10 mm. of the line of fracture it became more cancellous in structure and gradually darker in color until, directly opposite it, there was a wedge-shaped mass of cartilage with its base, measuring 5 mm., outward. On the periosteal side of the anterior aspect of the bone there was practically no callus excepting filling in the projection caused by the protrusion forward of the lower fragment. Here the newly formed bone was flush with the surface of the lower fragment and extended on the upper fragment 15 mm. In the medulla there was a small amount of new spongy bone on the sides of the cavity for 10 mm. on the lower and 5 mm. on the upper fragment. The entire line of fracture consisted of cartilage

Microscopic Description. Microscopic sections confirm the macroscopic description to a great extent. There was no bony union between the two fragments. There is dense fibrous tissue extending along the line of fracture opposite to the medullary canal. This contains leeshes of bloodvessels. At the internal angle between the two fragments there is a wedge of fibrocartilage which is continuous at the edge with osteoid trabeculæ. These are very thick at the internal angle and continue the general line of the bone. The periosteal trabeculæ are densest on the surface and have undergone great absorption, with the formation of wid ned spaces in the lower level of the callus. These spaces are filled with loose connective tissue, bloodvessels, small round cells, and osteoclasts. Where it borders on the cartilage there are especially large numbers of osteoclasts and in som e places the cartilage seems to be affected by them. In places it looks as if the cartilage were first eaten out by the osteoclasts, followed later by a deposit of lime salts at the margins of the cartilaginous trabeculæ. In other places it looks as if the cartilage were first penetrated by bloodvessels. There is considerable absorption of the cortex. Like the trabeculæ of the new callus, its spaces do not

appear to contain active osteoblasts, but are lined by flat cells.

There is only a small amount of osteoid tissue in the medullary cavity. The trabeculæ look as if they had been dense, but had suffered great absorption by osteoclasts. The medulla is congested with red blood corpuscles, but is not particularly cellular. There are no osteoclasts except in apposition with bone. There is a goodly number of leukocytes where there is absorption going on, so that they may have some connection with that process.

Experiment 23. Operation performed November 21, 1905. Animal died February 14, 1906. Fracture of eighty-five days' duration.

Macroscopic Description. The leg was found to be perfectly sound, having united with practically no displacement as far as could be determined without section through the bone. There was a moderate amount of firm callus present, extending 15 mm. on each side of the line of fracture. The callus on the anterior aspect was very red and vascular-looking; that on the postcior aspect, projecting about 7 mm., was deeply grooved by one tendon in particular, which had to be dug out of it. It was more lightly grooved by several others.

On longitudinal section of the bone it was found that there had been slight backward displacement of the upper fragment on the lower, with the formation of quite abundant periosteal callus, especially on the posterior aspect. This posterior callus was composed mostly of brownish, cancellous bone, with the exception of the portion nearest the old bone. Just below where the upper fragment ended it appeared as if condensation had taken place in order to take up the strain from the upper fragment. It contained very little cartilage. The periosteal callus on the anterior aspect contained a wedge of cartilage with a base of about 2 mm. and with its apex at the line of fracture. A thin layer of cartilage extended across the entire line of fracture. The periosteal callus on the anterior aspect contained more compact bone than that on the posterior aspect.

The medullary cavity was plugged with cancellous bone for about 15 mm. on each side of the fracture, beyond which the marrow was red in color.

Microscopic Description. The position of the fragments is good and there is abundant callus. Across the line of fracture there are intermingled islands of cartilage and osteoid trabeculæ, which are continuous with the osteoid trabeculæ in the medullary canal. On the periosteal aspect there is more cartilage to be seen, with a tendency to wedge formation. The most exterior portion of the callus next to the periosteum consists of a complete bridge of wide, osteoid trabeculæ, continuous from one fragment to the other. These spaces and the trabeculæ next to the cartilage are lined with osteoblasts. Most of the osteoid trabeculæ are quite dense, but there is some absorption by osteoclasts. This is especially marked in its deepest portion next to the old cortex, where it is forming an Haver-ian canal. The cortex has undergone some absorption, but the canals are not lined with osteoblasts.

The medulla is plugged with osteoid trabeculæ, on which are osteoblasts in some areas and not in others. There is little, if any, absorption of the medullary trabeculæ. The marrow is mostly of the hyperplastic variety, with an increase of connective tissue and some few cells. There are quite a number of polymorphonuclear leukocytes in other areas.

Experiment 24. Operation performed November 3, 1905. Animal killed February 9, 1906. Fracture of ninety-eight days' duration.

Macroscopic Description. The fracture was united, but the union was not bony. There was quite an abundance of callus present and some internal bowing at the site of fracture, with very slight rocking mobility.

On longitudinal section through the bone, anterior angularity of the fragments, with the formation of a very large periosteal callus on the posterior aspect, was found. This callus extended for 25 mm. on both fragments and was 10 mm. thick at its thickest part, opposite to the line of fracture. It was composed of dense, white bone; brownish, cancellous bone and cartilage, arranged as follows: The dense, white bone was farthest from the site of fracture for 8 mm., where it left the bone and continued on the outside of the callus as a layer, 3.5 mm. thick, to the edge of the cartilage, which was present as a wedge-shaped mass with its base (13 mm.) outward and its apex tapering to the line of fracture. The intervening space between the outer shell of hard bone, the cortex, and the cartilage was filled with cancellous bone. On the anterior aspect of the periosteal surface of the bone there was a small amount of callus consisting of a wedge of cartilage with its base (10 mm.) outward (4 mm. thick) and a tapering shell of white, dense bone 8 mm. long by 2 mm. at its thickest portion. The medullary cavity was completely closed for a distance of 10 mm. on each side of the line of fracture with spongy, brownish-white bone, which then gradually crept up the sides, fine trabeculæ being felt on the anterior aspect of the upper fragment 25 mm., and of the lower fragment 20 mm., from the site of fracture. They did not extend quite so far on the posterior aspect of the medullary cavity. There was a streak of cartilage, 2 mm. thick, extending across the medulla at the site of fracture. Beyond the new medullary bone there was red marrow for about 8 mm. and then yellow marrow. The nutrient artery pierced the upper medullary new bone.

Microscopic Description. Sections confirm macroscopic description with reference to osteoid tissue, position of fragments, etc. On the periosteal aspect of one side of the bone there is a great abundance of osteoid callus on each frag-

ment, separated by a wedge of dense fibrocartilage. The general trend of the canals in the osteoid tissue is almost vertical to the old cortex and the bone is very dense, excepting that in the lower levels of these masses there is great absorption (as described macroscopically) forming very wide canals parallel to the cortex. These canals contain loose connective tissue, osteoclasts, bloodvessels, and leukocytes. The outer layer remains dense, there being no absorption whatever. The fibrocartilage does not show much transition, but seems to have been separated from the neighboring tissue, leaving a space which is filled with a diffuse, slightly granular, eosin staining material. This extends almost entirely across the fragments.

On the other side of the fracture there is only a small amount of periosteal callus, which also abuts against a fibrocartilage wedge. Here, likewise, the osteoid tissue is dense, but instead of having undergone absorption in its deeper portions, more absorption has taken place in its superficial areas. Some of the spaces of the periosteal callus which have been caused by absorption are lined with apparent osteoblasts somewhat flattened out and not active.

The cortex has suffered great rarefaction by osteoclasts. The surface and ends of the fragments have undergone some absorption. The medullary cavity is partially filled with osteoid trabeculæ, which show considerable osteoclastic absorption. They do not appear to be covered with osteoblasts. The marrow is red in some places and contains some osteoclasts. There are no osteoid trabeculæ between the ends of the cortical portions of the fragments, but there appears to be almost the formation of a false joint, with very slight, if any, motion.

Experiment 25. Operation performed November 7, 1905. Animal died March 16, 1906. Fracture of one hundred and twenty-nine days' duration.

Macroscopic Description. Perfect union of the fracture was found with the formation of a very small callus which was slightly grooved for a couple of tendons. There was practically no displacement of the fragments as far as could be determined.

Longitudinal section through the bone demonstrated that the reposition of the fragments had been almost perfect, there being no displacement whatever. The line of fracture was distinctly visible and was completely filled with white, rather dense bone. On the periosteal side, extending for about 5 mm. on each side of the fracture, and for about 1 mm. in thickness, there was a layer of white, hard, new bone. There was no cartilage or dark, cancellous bone to be seen on the periosteal side of the bone. The medulla contained a very small area of very porous, reddish bone, apparently in the process of absorption, not extending entirely across the medullary cavity, and about 1 mm. in length. Running through its centre was the large nutrient artery. There was very slight forward angularity of the fragments.

Microscopic Description. The fragments are in perfect alignment, there being slight separation of the two ends on the one side. On both sides there is a small amount of periosteal osteoid callus which shows the general direction of the old spaces to be almost vertical, but there had been great absorption of the osteoid tissue with the formation of very large longitudinal spaces (Fig. 9). These spaces, in turn, are lined with new, dense bone, which takes brilliant eosin staining in contrast with the bluish stain of osteoid tissue. In addition, there is a striation parallel with the sides of the cavity, viz., formation of lamellæ. The cells are spindle shaped, as in old cortical bone. The periosteal osteoid tissue also has undergone considerable lacunar absorption on the surface. The cells, having been greatly destroyed or shrunken, it cannot be determined whether or not the spaces are lined with osteoblasts. The medullary cavity contains some scattered trabeculæ in the region of the fracture. Here, and to some extent up the sides of the bone, the marrow is red, but yellow elsewhere. There is great absorption of the cortex, especially at the line of fracture, where, in some sections, can be noted very large spaces which are beginning to show a deposit of new bone. On one site there have been formed distinct communications between canals of the cortex of both fragments, and the union is complete.

Experiment 26. Operation performed November 21, 1905. Animal killed August 10, 1906. Fracture of two hundred and sixty-two days' duration.

Macroscopic Description. The animal was killed after having been in the country for several months in order to keep its health up to a high standard, owing to the fact that long fractures could not otherwise be obtained since the animals died because of long confinement.

The leg was perfectly united and firm. There was a small-sized callus at the site of the fracture, but the alignment of the bone was very good. On removing the skin the callus was found to be grooved by the tendons passing over it. The length of the callus on the external surface was not over 12 mm.

On longitudinal section through the bone the position of the fragments was found to be very good. The line of fracture was still visible as a whitish line through the callus. At the line of fracture, in the small external callus and extending part way between the fragments, was a small area of cartilage. The remainder of the external callus was rather hard bone. The medullary cavity was completely filled with vascular-looking, cancellous bone continuous with the normal cancellous portion of the lower ends of the bone and extending above the line of fracture 2 cm. The nutrient artery entered the centre of it. Above the cancellous plug

was deep-red marrow. The plug of new bone was denser at the line of fracture than elsewhere. The ends of the fragments appeared somewhat darker than normal, looking as if there had been some absorption and it was intimately blended with the interposed callus.

Microscopic Description. There was almost perfect apposition of the fragments with a moderate external callus of osteoid tissue and a liberal plug of medullary osteoid tissue. In the external callus there are still remains of a wedge-shaped piece of cartilage or dense connective tissue, with evidences of its having extended across the entire line of fracture. In the specimens this is now a very small wedge on one side and is almost completely absent on the other side. The remainder of the periosteal callus shows superficial lacunar absorption and absorption of the deeper portions with the formation of medullary spaces parallel to the old cortex. The medullary cavity is filled partly with cancellous osteoid tissue which has suffered great absorption except near the line of fracture, where it is denser. The trabeculæ are thin and wide apart. The spaces are filled with red marrow which shows numerous osteoclasts. Some of the spaces contain fat cells also. There is great absorption of the cortex near the ends. At the line of fracture, where the two portions of the old cortex abut against each other, there are evidences, owing to the bluish character of the stain, of there having been originally fibrous tissue between the bones. This material is now replaced by osteoid trabeculæ containing more numerous and smaller spaces between them than other portions of the bone. These spaces unite with those of the old cortex, and the bone is practically healed. The spaces are lined by osteoblasts. The trabeculæ take a bluish-red stain.

Experiment 27. Operation performed November 7, 1905. Animal killed August 14, 1906. Fracture of two hundred and eighty days' duration.

This animal had also been in the country for several months.

Macroscopic Description. The leg was found to have apparently united very solidly, the animal having used it perfectly and there having been no mobility of the fragments. There was some nodulation felt at the site of fracture. On removing the skin there was found some callus extending up about one-half inch on each fragment, which was deeply grooved by the tendons that passed over it. The callus bound the tibia and the fibula tightly together.

On longitudinal section the periosteal callus was found to extend up on each fragment about 2 cm. and was about 1 cm. thick. It was composed almost entirely of a dark, vascular, porous, spongy bone divided in half at the line of fracture by a thin line of cartilage. This line of cartilage extended all the way across the medullary cavity. The medullary cavity was plugged completely for about 1 cm. on each side of the line of fracture with dense, white bone, beyond which (for about 12 mm.) there was porous vascular bone; beyond this, red marrow.

Microscopic Description. The fragments are in good position and there is abundant callus. On the periosteal side of the fracture there is a large, spindle-shaped callus showing thick trabeculæ with large spaces between them. These spaces are filled with marrow containing fat cells and marrow cells. The trabeculæ are dense in construction and take no particular direction, being very much like normal cancellous bone. The superficial surface shows considerable osteoclastic absorption.

In the medullary cavity there are similar trabeculæ for some distance on each side of the line of fracture. The trabeculæ are not so thick and the spaces between them are slightly larger than in the periosteal callus. There is considerable absorption of the cortex at the ends and in its substance generally, the widened spaces communicating freely with those of the periosteal and medullary trabecular spaces. The marrow is not present in great abundance and is more cellular than normal, but not red.

At the line of fracture, extending across the entire mass, is a moderately thin layer of dense fibrous tissue and fibrocartilage. In areas this shows transition into osteoid trabeculæ. In other areas it has a diffuse hyaline appearance, taking the eosin stain. There is no angular displacement and no wedge of cartilage, merely a thin strip in the periosteal callus.

SERIES 3.

This series, performed upon dogs, had for its object the determination of the activities of the various portions of the bone independent of extrinsic forces. Each operation consisted in making an incision over the tibia to the bone and then making a sawcut half-way through the bone in order to injure all the elements of the bone as in fractures, but with none of the attendant displacement of the fragments, etc. The skin was then sutured and the leg placed in a shaped splint and wrapped with a sodium silicate bandage.

Experiment 28. Operation performed September 15, 1905. Animal killed September 20, 1905. Fracture of five days' duration.

Macroscopic Description. The wound appeared to have healed by first intention, but on considerable pressure there was an escape of a small drop of thin, yellow, serous fluid between the stitches. There were signs of ecchymosis around the wound and down the leg to the ankle. On removal of the skin, considerable ecchymosis was found in the region of the wound, but no infection was apparent. The sawcut appeared to be filled in with a gelatinous, pinkish-white material. There was no free, unorganized blood present.

Longitudinal section through the bone revealed the fact

that the sawcut had been made almost directly opposite to the point of entrance of the nutrient artery into the medullary cavity. The sawcut was filled flush with the surface of the bone with a brownish, fairly firm material. The periosteum above the wound appeared to be a little thickened, but there was no callus. In the medullary cavity, almost completely filling its lumen, there was a white, glistening mass that appeared to be young callus, next to which was red bone-marrow. The remainder of the marrow at the lower end was yellow. Above the periosteum there was a blood clot.

Microscopic Description. The sawcut proved to have been made just at the junction of the cancellous and the compact bone. In making it, a sliver of bone was bent and forced into the medullary canal. The periosteum has not proliferated, but the tissues are infiltrated with blood. The sawcut is filled with blood clot and no formative cells appear to be present.

In the medulla at the site of the wound, and filling almost one-half the lumen of the canal, there is a very loose cellular connective tissue, much like myxomatous tissue. This appears to arise from the connective tissue between the fat cells, for at the outer edge of the mass it can be noted that fat cells are gradually decreasing in number and the intercellular substance increasing until the fat cells and the small, round, eosinophilic medullary cells become entirely obliterated.

Embedded in this mass of tissue is a broken or bent-off spicule of old bone, on the surface of which are large polygonal cells. New trabeculæ are apparently formed by these cells secreting a homogeneous matrix which is strongly eosinophilic and which finally includes some of the cells in the mass.

On the medullary surface of the cortex, the endosteum can be seen to thicken on each side of the sawcut and to form polygonal cells which also form trabeculæ in the same manner. The cortex in the neighborhood of the wound shows dilated Haversian spaces, but that these are normal, being the beginning of the formation of cancellous tissue and not due to absorption, is shown by the arrangement of the bone cells around their outskirts. These spaces also contain osteoblasts and trabeculæ. There is no absorption and no phagocytes are present. The marrow is slightly cellular.

Experiment 29. Operation performed September 28, 1905. Animal killed October 5, 1905. Fracture of seven days' duration.

Macroscopic Description. The wound had united perfectly, but was encrusted with a yellowish material like pus and a little pus came out of one stitch-hole on pressure. On removal of the skin, no pus was found in the deeper tissue. There was nothing covering the sawcut, which was partially filled with a whitish material. The periosteum was slightly thickened.

On longitudinal section, the periosteum was found to be thickened below and above (but not within 1 cm. above) the sawcut. The sawcut was one-fourth filled with a yellowish-white material which was not very hard. The medulla appeared to be condensed for about 2 cm. in the region of the sawcut, which had been made about 1 cm. below the point of entrance of the nutrient artery into the medullary cavity.

Microscopic Description. The sawcut is about half-filled with round cells the nature of which cannot be accurately determined, *i. e.*, whether they are leukocytes or marrow cells. The periosteum at some distance from the wound has increased slightly in thickness, with the formation of large, polygonal, formative cells in the lower layers. There is no evidence whatever of trabeculæ formation. There are no signs of cartilage. The superficial surface of the cortical bone has upon it pits or depressions, the result of phagocytosis by osteoclasts which are found lodged in them. There does not appear to be any widening of the Haversian spaces.

The marrow is of the red cellular variety and, in the region of the wound, the endosteum is thickened, with the formation of large polygonal osteoblasts. These are found extending to the centre of the medullary cavity opposite to the wound. Among these masses of cells can be seen a transition into osteoid trabeculæ by the secretion of a hyaline matrix, with a rearrangement of the cells so that they lie as a layer on the newly formed trabeculæ. They extend almost completely across the wound in the form of an arch. A few separate fragments in the medulla are being absorbed by osteoclasts. There are no trabeculæ in the sawcut and no absorption of the sides of the cut. Large multinuclear cells are present in the medulla.

Experiment 30. Operation performed September 8, 1905. Animal killed September 16, 1905. Fracture of eight days' duration.

Macroscopic Description. The wound was found to have united by first intention. On removing the skin practically no callus could be seen, but the sawcut was filled with a reddish, gelatinous material.

On longitudinal section through the bone, the periosteum was found to have proliferated very little if at all. On the medullary side of the sawcut here was a condensation of the medulla and, at one place, there was new bone formation projecting into the medullary cavity. The sawcut was on the opposite side of, and about 7 mm. lower than, the entrance of the nutrient artery into the medullary cavity.

Microscopic Description. Examination with the lower powers shows that in none of these sections had the sawcut penetrated quite into the medulla, that area probably being in the other half of the bone preserved for grinding. That the cut must have penetrated the medulla is demonstrated (?) by the fact that there is marked reaction in the medullary cavity in the region of the sawcut.

There is a small amount of fibrous thickening of the periosteum, but no proliferation of the osteogenetic or deeper layers is noticed excepting in small areas, where the smooth external surface of the cortical bone has been eroded by osteoclasts. Here there appears to be a reaction in the periosteum.

The endosteum does not show much reaction except in the region of the sawcut, where there is a new formation of osteoid tissue with its large cells containing large nuclei. The trabeculæ are covered with large polygonal osteoblasts. This new bone mass projects into the lumen of the medullary cavity about one-fourth the distance across the canal. The hyperplastic marrow in the same region shows numerous osteoclasts or polynuclear, brown-staining cells. The remainder of the medulla is of the red variety, with its eosinophilic, variously sized, brown, mononuclear cells. The bone shows practically no reaction, the spaces not being dilated and containing no proliferating cells.

Experiment 31. Operation performed July 24, 1905. Animal killed August 2, 1905. Fracture of nine days' duration.

Macroscopic Description. The wound had healed by first intention. On removal of the skin, the wound in the bone was found not to have been entirely filled with callus.

Microscopic Description. The sections demonstrate that the sawcut had been made just where the cancellous joins the compact porton of the bone. There is no proliferation of the periosteum except to a very slight degree where the cortex appears to be eroded.

The endosteum does not appear to be proliferated excepting over the trabeculæ of the old cancellous bone. The medullary tissue is red on the margins and then, as one approaches the sawcut, becomes more admixed with young connective tissue. In the immediate neighborhood of the sawcut are delicate trabeculæ of osteoid tissue covered by osteoblasts. This osteoid tissue extends above and below the sawcut and half-way across the medullary cavity. It also extends upward into the sawcut for about half its depth, where it becomes mostly cellular connective tissue with spindle cells and some young, thin-walled bloodvessels. On the periosteal side of the wound, the sawcut is filled with fibrillated fibrin streaming out of the wound. There is no cartilage. There is slight absorption of the cortex present.

Experiment 32. Operation performed July 24, 1905. Animal killed August 3, 1905. Fracture of ten days' duration.

Macroscopic Description. The wound had healed by first intention. On removing the skin, at the site of the bone wound there was found a very minute quantity of a reddish-yellow, turbulent fluid which appeared to be debris of blood clot, etc. At the site of the fracture there was a moderately firm, reddish-yellow accumulation of material for about 6 mm. in extent.

On longitudinal section it was found that the sawcut had entered the medullary cavity, which was filled with callus for over 6 mm. above and below the sawcut. The callus was rather firm. Owing to the muscle, etc., it was difficult to state how much callus was formed on the periosteal side.

Microscopic Description. There is some debris present with some slight inflammatory reaction but probably no marked infection. The wound is filled with dense granulation tissue with granular debris on the top. There is marked thickening of the periosteum with the formation of a fairly thick layer of osteoid tissue all around the bone excepting in the immediate neighborhood of the wound, where there is no callus. The periosteal process of bone formation is shown clearly. The periosteum is raised up. Both layers, the fibrous and the osteogenetic, are thickened. The osteogenetic layer is composed of large cells with large vesicular nuclei. These cells show the deposition, in parallel lines, of a homogeneous eosin staining material in the matrix between the cells. This material accumulates in greater bulk and includes some of the cells in its substance, while other cells are arranged in layers on the surface of the trabeculæ. Still others lose their polygonal shape and become more or less spindle shaped, forming the medullary tissue between the trabeculæ. Deeper down the trabeculæ are much thicker and the spaces between them much smaller, showing that they are older and demonstrating the action of the osteoblasts in their formation. The periosteum must have been subject to considerable chemical or toxic irritation to cause this profuse growth of osteoid tissue, for there was not much mechanical irritation present. The medullary cavity is filled across the entire lumen, and for about 12 mm. on each side of the wound, with loose osteoid trabeculæ, distributed in greater part, in irregular clumps, the outlines of which are defined by connective tissue or bloodvessels. In the medullary spaces between the trabeculæ are many fat cells. The osteoblasts are not arranged in many places, as usual, in layers, but are irregularly placed and blend directly with the trabeculæ. The gradual thickening or proliferation of the tissue between the fat cells, with the gradual deposition of osteoid tissue in this proliferated tissue, appears like cause and effect. The endosteum also shows thickening, with a deposition of trabeculæ on the inner aspect of the cortex, but not to a very great degree.

There is slight widening of the Haversian spaces of the cortex, but no lacunar absorption or proliferated tissue in the dilated spaces. There is lacunar absorption by osteoclasts of the sides of the sawcut (Fig. 12) and on the periosteal aspect of the cortex next to the sawcut. The cut itself is filled with granulations which are rather dense and vascular in the more superficial portions. In the deeper portions, toward the medulla, this granulation tissue is blended with

the proliferated tissue of the medulla, from which it probably takes origin. It differs in that the cells are more spindle shaped, and more closely packed. Toward the medullary side of the sawcut, parallel with its edge and in the direction of the streams of granulation tissue, can be seen trabeculæ (Fig. 12) forming in the proliferated tissue. Large multinuclear cells are found in the marrow.

Experiment 33. Operation performed August 18, 1905. Animal killed August 29, 1905. Fracture of eleven days' duration.

Macroscopic Description. The wound had healed by first intention. There was a small amount of external callus at the site of the wound and the sawcut was somewhat filled in.

Microscopic Description. In the medullary cavity there is abundant callus in the form of rounded masses, separated almost opposite the sawcut by large bloodvessels around which there are no trabeculæ. They unite at the base of the sawcut and are continued into it almost to the surface, in the centre of a mass of cellular fibrous tissue. The trabeculæ enter the sawcut from the medullary cavity, forming vertical columns parallel with the edges of the wound, with no attachment to the sides of the cut. The connective tissue surrounding the trabeculæ contains numerous multinuclear giant cells. The medulla is of the red variety and blends with the osteoblastic tissue forming the trabeculæ. It is also found in some of the medullary spaces between the trabeculæ. Covering the trabeculæ, usually in a single layer, are very large polygonal cells with vesicular nuclei. These blend with the connective tissue filling in the wound.

The periosteum is thickened with the formation of trabeculæ in its deeper layer. These trabeculæ decrease as the sawcut is approached and disappear at its edge. There is possibly some absorption of the cortex, but this is questionable. Its spaces are not lined with osteoblasts. There is no absorption of the periosteal trabeculæ or of the superficial surface of the cortex.

Experiment 34. Operation performed September 7, 1905. Animal killed September 19, 1905. Fracture of twelve days' duration.

Macroscopic Description. The wound had healed by first intention. On removing the skin at the site of the operation, there was no external callus to be seen, but the sawcut appeared to be filled in with a reddish-white, gelatinous material.

On longitudinal section of the bone, considerable thickening of the periosteum was found, but it was soft in consistence. The sawcut was half-filled with a firm, dull-white material, probably cartilage, which extended over one-half the distance across the medullary cavity for 15 mm. in length.

Microscopic Description. The sawcut is found to have entered the medullary cavity about 6 mm. below the entrance of the nutrient artery. The thickening felt in the periosteum is mostly of the fibrous layer, although above the sawcut, beginning at a little distance from the wound, there is a thin layer of periosteal osteoid bone formation which gradually becomes thicker and then thinner again. It has no connection with the wound.

There is a large amount of osteoid trabeculæ in the medullary cavity, the material that had appeared like cartilage being osteoid in character. This osteoid tissue extends across the lumen until it encounters the nutrient artery, which courses across the medullary cavity in a diagonal direction from above downward. This results in the formation of more osteoid tissue above than below the sawcut. The artery acts as a barrier to the formation of the osteoid tissue, as practically none is to be found at the other side of the vessel except at the point of entrance of the artery. It is difficult to state whether the osteoid tissue originates from the endosteal membrane, for that does not show exceptional thickening. The marrow itself appears to have more relation to it, there being a hyperplastic condition of the connective tissue, in addition to the fact that, on the outskirts of the callus, it is of a red, cellular variety.

The cortex exhibits some widening of the Haversian spaces, but only a very small amount of lacunar absorption with but few osteoclasts. Some of the dilated spaces may be due to its proximity to the normal cancellous tissue. They are not lined with osteoblasts. The sawcut is filled, in its lower or internal three-quarters, with osteoid trabeculæ originating from the medulla. Its upper portion is filled with blood debris, leukocytes, and phagocytes (large multinuclear cells which do not take the usual brown protoplasmic stain of osteoclasts, but more the color of blood cells). Sections where the cut has not entered the medulla show no trabeculæ. The trabeculæ in the wound go in a vertical direction, that is, parallel with the axis of the cut. The cortex edges and periosteal surface, in places, have undergone lacunar absorption by osteoclasts. All the osteoblasts are very large. There is no absorption of the periosteal trabeculæ. There are some very large multinuclear cells in the marrow.

Experiment 35. Operation performed August 30, 1905. Animal killed September 14, 1905. Fracture of fifteen days' duration.

Macroscopic Description. The wound had healed by first intention, but there was not a great amount of external callus present. On removing the skin there was some slight evidence of an old blood clot, and a small amount of callus was present at the sides of the sawcut.

Longitudinal section revealed practically no external callus, but the sawcut was filled with young bone, which occupied the medullary cavity for a space of about 1 cm. in the region of the bone wound. Next to this was an area of cartilaginous callus and then normal medulla.

Macroscopic Description. There is no osteoid periosteal proliferation whatever in the celloidin sections, but the ground specimen shows, on one side of the sawcut, a moderate amount of osteoid trabeculæ. In the medullary cavity osteoid trabeculæ extend from the region of the wound almost completely across the medullary cavity and up and down from the sawcut for some distance. The endosteum is thickened and there is new bone formation lining the inside of the cortex on both sides of the canal. The layer of osteoblasts is thin. The principal and characteristic portion of the specimen is the changes that are to be noticed in the medulla. On the outskirts of the new bone growth the medulla is more cellular than normal yellow marrow. Then there appears a proliferation of connective tissue between the fat cells. This becomes gradually thicker and denser and arranges itself in the form of a more or less wide-meshed network (Fig. 13), in the same manner as the osteoid trabeculæ; that is, there is not a new cellular growth around every fat cell, but merely around groups of cells. This fact is brought out by both ground and celloidin sections. In a great measure the osteoblasts are not definitely arranged, but the bone formation is apparently by transformation of connective tissue (?). There is no absorption and no osteoclasts are apparent. Young, thin-walled bloodvessels are growing into the spaces between the trabeculæ. The oldest trabeculæ are in the region of the wound and what, on gross examination, appeared to be cartilage is young cellular trabeculæ in which there has been but little calcium salts deposited. This is demonstrated by the ground specimen.

The sawcut is, for the most part, filled with osteoid trabeculæ. These arise from the medullary cavity, as shown by their vertical arrangement and by the fact that, in the portions of the specimen where the wound had not entered the medulla, there are few, if any, osteoid trabeculæ, the wound being filled by connective tissue. The Haversian spaces in the cortex are possibly slightly dilated, but there are no proliferative changes in them.

Experiment 36. Operation performed August 30, 1905. Animal killed September 15, 1905. Fracture of sixteen days' duration.

Macroscopic Description. The wound had healed by first intention. On removing the skin a small amount of callus was found at the site of operation. On longitudinal section through the bone, the sawcut was found opposite to, and 10 mm. farther up than, the entrance of the nutrient artery into the medullary cavity. The main branch artery to the upper portion of the tibia was pushed aside by the new bone formed in the medullary cavity. The sawcut was filled flush with the surface by new bone, which appeared to be cancellous in structure. There was a thickening of the periosteum which did not appear to be very firm and which did not contain new bone. On the endosteal side of the cut, the almost transparent, brownish-white, new bone formation almost occluded the lumen of the medullary cavity and extended on both sides of the cut 4 mm. Outside of this there was a very thin layer of whitish material, then red marrow with yellow marrow nearer the ends.

Microscopic Description. Only one of the celloidin sections contains a slight periosteal new bone formation. The remainder show some lacunar absorption on the surface of the cortex with, possibly, some proliferation of the osteogenetic layer of the periosteum. In the ground specimen, there is a moderate amount of periosteal new bone formation which diminishes as it approaches the sawcut and terminates at it. The sawcut is made in the portion of the bone where it is beginning to become cancellous, so that the Haversian spaces of the cortex are large. However, there is lacunar absorption by osteoclasts and in some of the spaces there are layers or sheets of large polygonal cells like osteoblasts. In some there are red marrow cells. Whether or not these spaces are the result of the fracture it is impossible to say.

The medulla is almost completely filled with osteoid trabeculæ for some distance above and below the sawcut, but not beyond the artery, which is either shoved to one side or has limited the growth of the trabeculæ. The trabeculæ are thin and covered by osteoblasts and the medullary spaces between contain young bloodvessels. In the medulla there is a formation of the connective-tissue trabeculæ that precede osteoid trabeculæ. The whitish area seen on gross examination is not cartilage, but probably connective tissue or osteoid tissue before calcareous deposition has occurred. The sawcut is filled with trabeculæ, the general trend of which is parallel to the sides of the cut. There is a great amount of lacunar absorption of the edges of the wound.

Experiment 37. Operation performed September 5, 1905. Animal killed September 22, 1905. Fracture of seventeen days' duration.

Macroscopic Description. The wound was granulating at the upper end, but there was no suppuration present. On removing the skin the granulating area was found to be bound down to the bone and was cut away. At the site of the operation, which was high up in the cancellous part of the bone, there was evidence of a small amount of callus and no evidence of the sawcut. On longitudinal section, the sawcut was found to have been made opposite to and 5 mm. higher up on the bone than the entrance of the nutrient artery into the medullary cavity. The sawcut was almost completely filled by a new bone formation which greatly resembled the old bone. There was a new formation on the endosteal side, extending not quite 1 mm. into the lumen of the cavity and extending lengthwise for about 6 mm.; 5 mm. above the sawcut, and on the outside of the bone, is new periosteal bone formation 10 mm. long and 1.5 mm. thick. Below the sawcut there was also very slight bone

formation, making a hollow at the site of the operation. The periosteum was thickened all over. The marrow was red in the upper third and yellow below. It was extremely difficult to determine which was new and which old bone. The old bone was 1.5 mm. thick.

Microscopic Description. The sawcut is far up on the cancellous tissue, where the cortical covering is thin and riddled with large medullary spaces. These are filled, especially those near the medullary cavity, with cosinophilic medullary cells, bloodvessels, and loose connective tissue almost myxomatous in nature. The periosteum, above and below the sawcut, shows a rather liberal amount of osteoid trabeculæ, the axes of which are very oblique, so that they are almost parallel with the line of the bone. The spaces between them communicate in part with the Haversian canals of the cortex, as shown by the ground specimen (Fig. 14). It is probably in this manner that the bloodvessels enter the newly formed medullary spaces. Compared with that in other similar experiments, the endosteal new bone growth is small in amount, extending but a short distance into the lumen of the canal. It extends farther up and down on the inner surface of the cortex. The marrow is red, being very cellular against the new trabeculæ. There does not appear to be much connective-tissue overgrowth.

The cortex is riddled with large spaces, in some of which the continuation of the endosteum has proliferated, forming a single layer of large polygonal cells. Others contain osteoid trabeculæ, just as in the medullary cavity proper. There are some very large osteoclasts present, but there does not appear to be a great amount of lacunar absorption. The sawcut is filled with osteoid trabeculæ which appear to be derived from the widened Haversian spaces as well as from the endosteum itself. The trabeculæ are more in the form of a network, with wider spaces between them in those cases in which they are derived only from the endosteum, and they are vertically and closely arranged. It appears as if there is less new formation in the medullary canal because of the natural porosity of the region and because the physical nature of the bone does not require such a thick callus, and also owing to the fact that the cortex itself is thickened by new trabeculæ.

Experiment 38. Operation performed September 10, 1905. Animal killed September 29, 1905. Fracture of nineteen days' duration.

Macroscopic Description. The wound had united by first intention. On removing the skin at the site of operation, a small amount of callus, not very firm in consistency, was found. Apparently there was no new bone formation.

Longitudinal section through the bone showed that the sawcut had been made opposite to, and 3 mm. above, the entrance of the nutrient artery into the medullary cavity. The sawcut was filled with firm, white bone, whiter than the remainder of the leg. On the endosteal side there was a mass of callus or newly formed bone 7 mm. in length and extending over one-half the lumen of the medullary cavity, somewhat more above than below the site of the operation. On the periosteal side there was some thickening of the tissue, but no new bone.

Microscopic Description. Owing to some improper position during cutting, one end of the specimen above the sawcut consists of nothing but solid cortical bone, with no medullary cavity. The sawcut had penetrated into the medullary canal and there was a large amount of new bone formation in the medullary cavity around it, extending up into the cut flush with the surface of the bone. The bone cells in the new trabeculæ are much more abundant and have the polygonal shape of osteoblasts, differing from the spindle shape noticed in adult bone. The older of the newly formed trabeculæ contain cells more like old cortical bone cells than the younger trabeculæ, in which the cells are not compressed. The trabeculæ appear more fibrillated than usual.

The periosteum contains some osteoid bone formation, and at the edge of the wound there is a small connecting ridge between the periosteal and endosteal bone which becomes continuous. At the level of the surface of the bone the trabeculæ in the sawcut show their method of formation, having cells only partially embedded in homogeneous osteoid material (Fig. 15).

In the cortex are large Haversian spaces with little proliferation of the tissue contained therein. Some of them are due to lacunar absorption by abundant osteoclasts, especially near the periosteal surface, and some appear natural, as shown by the disposition of the bone cells around them. The marrow is not well stained.

Experiment 39. Operation performed August 29, 1905. Animal killed September 20, 1905. Fracture of twenty-two days' duration.

Macroscopic Description. The wound had healed by first intention. On removing the skin no firm callus was found, but there appeared to be some thickening of the tissues in the neighborhood of the fracture.

On longitudinal section, the sawcut was found entirely filled in with a white, somewhat dense bone. On the periosteal side of the bone there was a new formation of quite compact bone above and below the sawcut, not quite 2 mm. in thickness at its thickest part. It extended upward for almost 10 mm. and downward for 5 mm., with its thickest portion about 3 mm. above the sawcut, which was filled almost flush with the level of the old bone. On the endosteal side of the cut the new bone was more cancellous and of a reddish-white color. It extended into the lumen of the medullary cavity for 2 mm. and was 10 mm. in length. The innermost shell of bone was more compact than the portion be-

tween it and the sawcut. The marrow was deep red in color excepting a very small amount at the lowermost portion.

Microscopic Description. The sawcut was made at about the junction of the cortical and cancellous bone. The periosteum shows a moderately thick layer of osteoid bone formation which extends to the sawcut and unites with that in the cut, both projecting above the surface of the old cortical bone. The periosteal new bone is very dense and the medullary or Haversian spaces between the trabeculæ are very long and narrow, running almost parallel to the old cortex. They intercommunicate with one another and with the cortex of the old bone. In the ground and cut specimen there appears to be an especially large Haversian space at the point of union of the periosteal and cortical bone, giving branches of communication to both. It shows practically no absorption.

On the medullary side of the cut there is a fair amount of osteoid bone formation which has undergone great absorption, especially on the inner margins of the mass. The phagocytic multinuclear osteoclasts are so large and so abundant as to almost form continuous layers (Fig. 16). The effects of the absorption can be seen in the form of lacunæ and large medullary spaces filled with red marrow. The surrounding marrow is red and vascular, with many free red blood corpuscles. The medullary spaces in the new medullary bone communicate freely with the old cortical Haversian spaces.

There is very great absorption of the cortical bone, the Haversian spaces being much dilated and containing abundant osteoclasts and some formative cells. Much of the tissue contained therein is almost mucoid in nature. The absorption at the saw wound is so extensive and deep that if forms communications (Fig. 17) between the old Haversian spaces and the new intertrabecular medullary spaces of the sawcut. The general trend of the trabeculæ in the sawcut is at right angles to the bone, while those of the periosteum are parallel with its axis. At the point at which they unite, neither direction is maintained, but large, irregular spaces are formed. Osteoblasts do not appear active in any other situation, and even here there is not much new bone being formed. The periosteal new bone is denser than the old cortex.

Experiment 40. Operation performed August 17, 1905. Animal died September 18, 1905. Fracture of thirty-two days' duration.

Macroscopic Description. The wound had united by first intention. On removing the skin the site of the bone wound was found to be perfectly clean, but there was not an abundance of callus present. The sawcut was completely filled in with callus.

Longitudinal section through the bone showed the operative wound to have been almost at the junction of the cancellous and the compact portion of the bone. It was located almost opposite the entrance of the nutrient artery. The sawcut was completely filled with newly formed bone, which spread out on the other side of the medullary cavity so that, on section, the whole formation of bone had the appearance of a funnel. Next to the bone there was an area of reddish, rather firm material and then normal medulla.

Microscopic Description. The sections confirm gross examination as to the situation of the sawcut. There is a layer of callus, not of great thickness, in the periosteum above and below the cut. There is an especially large new Haversian canal present just superficial to the old cortex. The remainder of the new bone is fairly firm. Where it unites at the sawcut with the bone filling that area, there are some signs of absorption and irregularity.

In the medullary cavity there are osteoid trabeculæ extending into the lumen of the canal. These trabeculæ are wider apart and more irregular in shape than when first formed. They show signs of great absorption, being covered, in areas, by osteoclasts. These large phagocytes appear to remove the salts and liberate the bone cells intact, for in some areas the cells are one-half surrounded, the other half free and other cells seem to have been just freed. These bone cells, when liberated of their rigid surroundings, appear as moderately large mononuclear cells with small round, deeply staining nuclei and a fair amount of a rather poorly staining protoplasm. They resemble greatly normal nucleated marrow cells. The medullary spaces between the trabeculæ are very vascular and there seems to be much free blood. After the absorption of the salts the framework of the bone appears to be a loose connective tissue very much resembling its condition before calcification. This is shown in the outlying district of the new bone, in which the arrangement of the bloodvessels demonstrate that there had probably been trabeculæ present which had been absorbed. This gave the reddish, rather firm, material described above. The marrow is of the red vascular variety.

In the cortex there is a moderate amount of absorption, but not quite as much as might be supposed. There do not appear to be quite so many communications between the old and new Haversian spaces as in the previous specimen.

Experiment 41. Operation performed September 19, 1905. Animal killed November 28, 1905. Fracture of seventy days' duration.

Macroscopic Description. The wound had healed perfectly by first intention. On removing the skin, there was found, at the site of the operation, a nodule about 6 mm. in diameter.

Longitudinal section through the bone did not strike the medullary cavity throughout its entire length, but the sawcut was completely filled with hard white bone and there ap-

peared to be some brownish, spongy bone still present in the medullary cavity.

Microscopic Description. The sawcut is healed entirely and the reparative processes in the bone have subsided greatly, there being much less activity than is seen in the early stages of repair. On the periosteal aspect there is a rather thick, very compact layer of new bone which is continuous over the sawcut as a regular surface without a depression. The external aspect shows very marked lacunar absorption (Fig. 18), the lacunæ containing osteoclasts and being filled with young cellular connective tissue. It is impossible to give the fate of the bone corpuscles, as they are liberated from the bone. They are seen first as small round cells with a small amount of protoplasm next to the bone. A little farther off only deep-blue nuclei can be seen in the midst of connective tissue. Finally, there is no sign of them whatever. Whether they degenerate and disappear or whether they go to form new connective tissue it is impossible to state, but the former seems to be the more probable. The Haversian spaces in the periosteal bone appear more like the normal Haversian spaces, being narrow and branched. In the larger ones the osteoblasts, which are still present on the sides of the canals, have lost their closely packed, polygonal arrangement, and appear more like normal medullary cells, being round, with a fair amount of indifferently staining protoplasm and a single, small, round nucleus. They look also like liberated bone cells.

The medullary cavity contains some remaining trabeculæ which are undergoing absorption, but by no means as actively as in some of the previous experiments. Some osteoclasts are present, but not in great abundance. Red cellular marrow fills in all the medullary spaces.

The sawcut is interesting and instructive. It is completely filled with more or less compact bone in which the trend of the medullary or Haversian spaces has changed from at right angles to the long axis of the bone to a direction parallel with it. Differences in staining demonstrate how the old vertical spaces had been filled in and then new transverse spaces made which were larger at first than now. There has been a new deposit of bone in both the widened canals of the old cortex and the new bone, so that an effectual union has been formed between the old and new bone. As a result of this the new bone does not separate from the sides of the cut as in previous specimens. Often, in one area, bone of three stages of development can be seen, viz., the old cortex, old new bone, and recent new bone formation (Fig. 19). The corpuscles of this later new bone are more spindle shaped and the bone appears denser and more like the normal cortex than is the case with the older osteoid bone. Osteoblasts are not present in layers, but there appear to be more marrow cells, as described under the periosteum. All the cells look smaller than in the early active stage of proliferation.

SERIES 4.

This series, performed upon dogs, had for its object the determination of the activity of the cortex and medulla when deprived of the coöperation and assistance of the periosteum. Each operation consisted in making an incision over the tibia to the bone, reflecting the periosteum for about a half-inch on each side of the proposed cut, removing it, and then making a sawcut in the bone deep enough to enter the medullary cavity. The external wound was sutured and the leg placed in a splint and wrapped in a sodium-silicate dressing.

Experiment 42. Operation performed September 19, 1905. Animal killed September 24, 1905. Fracture of five days' duration.

Macroscopic Description. The wound had healed by first intention except at the upper angle, where a stitch had pulled out. On removing the skin, no callus was found, but the sawcut was filled with a soft, reddish material. The bone surface from which the periosteum had been denuded was granular-looking, with little crypts in it as if in a state of osteoporosis.

Longitudinal section through the bone demonstrated that the sawcut had been made opposite to, and about 2 mm. below, the entrance of the nutrient artery into the medullary cavity. The sawcut was only partially filled with a reddish-white, fairly firm material. On the endosteal side, for about 8 mm. in length and almost filling the lumen of the medullary cavity, was a rather firm, reddish-white mass, probably young callus, surrounded by a zone of reddish marrow. The periosteum was absent.

Microscopic Description. The Haversian spaces throughout the bone are very large, the cortex being comparatively thick and porous for its size. The periosteum had been effectually removed on the side of the cut, but on the opposite side of the bone and beyond the limits of its removal it gave evidences of some activity, the smooth surface of the cortex exhibiting lacunar absorption and the deeper layers of the periosteum showing some hyperplasia.

On the superficial surface of the sawcut are fibrin and red blood corpuscles. Deeper down are loose connective-tissue cells with what appear to be marrow cells; and deeper still are some young osteoid trabeculæ with large osteoblasts covering their surfaces and containing large polygonal cells. These young trabeculæ appear to spring from the sides of a very large Haversian space, which communicates directly with the medullary canal and is lined with endosteum. The medullary canal contains some young trabeculæ springing from its sides in the immediate neighborhood of the sawcut. All these trabeculæ are attached to the sides of the bone and do not connect with or bridge over to one another. They are all covered with large osteoblasts, which

are directly continuous with the single layer of polygonal cells lining the sides of the medullary canal for some distance from the sawcut. This is the hypertrophied endosteum.

The marrow in the region of the new tissue is very red and cellular, and in the region of the trabeculæ shows an increase of loose connective tissue. It contains numerous polynuclear cells (osteoclasts). The cortex contains large dilated Haversian spaces filled with bloodvessels, marrow cells, and loose connective-tissue cells. It is thick and has undergone some absorption by osteoclasts. It is evidently still in the process of development, as the animal was only a pup. This absorption is general and does not appear to have any connection with the fracture.

Experiment 43. Operation performed September 15, 1905. Animal killed September 22, 1905. Fracture of seven days' duration.

Macroscopic Description. The wound had healed by first intention. On removing the skin no external callus was visible. The periosteum had apparently regenerated. The sawcut was plainly visible and was filled with a reddish, soft material.

On longitudinal section through the bone, very little change was found in the medulla, as the sawcut appeared to have scarcely entered the medullary cavity. The marrow was yellow and the compact bone was very thin. There was no periosteum present.

Microscopic Description. The sawcut has barely entered the medullary cavity, pushing before it for a short distance into the canal the last thin piece of bone. However, it has traversed a couple of large Haversian spaces, which are filled with red medulla, as the sawcut has been made up near the cancellous portion of the bone. The result is the same as if it had wounded the medulla to a greater extent.

The periosteum is absent and there is no activity or absorption of the superficial portions of the bone. The medullary canal shows red marrow on the sides of the cavity, especially thick in the region of the sawcut. There is also a very thin deposit of new bone on the inner aspect of the cortex, with some proliferation of the endosteum.

The large Haversian space immediately adjoining the medullary canal shows thickening of the endosteum, with the formation of new trabeculæ, more or less fibrous in nature and covered with osteoblasts. The space contains red marrow cells. The sawcut is filled with loose connective-tissue cells, some marrow cells, and trabeculæ.

Experiment 44. Operation performed September 24, 1905. Animal killed September 30, 1905. Fracture of nine days' duration.

Macroscopic Description. The wound was found to have healed by first intention. On removing the skin there did not appear to be any callus at the site of the operative wound, but the sawcut was filled flush with the surface of the bone with a somewhat soft, whitish material.

Through some oversight in sectioning the bone longitudinally, it was taken in the wrong direction, so that the entire operative area was in one-half of the bone. The section was cut in half through the sawcut and preserved for embedding in that manner. There was thick, white tissue on the outside and thickening in the medullary cavity in the neighborhood of the wound, but no new bone formation. The operative wound was half-filled with a rather firm, white material.

Microscopic Description. The sections were made through one-half of the bone opposite to where the operation was performed, so that the cut was not in the section at all. There was no periosteal proliferation to be seen. The medullary cavity contains bone formation on the inner aspect of the cortex, projecting into the lumen of the canal for a short distance, with some cellular marrow in its neighborhood. In the centre of the canal, in some of the sections, there are a few osteoid trabeculæ, demonstrating that the nodule that was present at the site of the cut had extended over half the distance across the canal. The specimen shows beautifully the filamentous connective tissue between the fat cells (Fig. 11) on the outskirts of the mass of osteoid trabeculæ, illustrating how this increases in quantity, gradually obliterating the fat cells and then becoming converted into osteoid trabeculæ by the invasion of the osteoblasts and a deposition of calcareous salts. In the ground section osteoid trabeculæ fill in the sawcut, but there is no periosteal activity and no cortical changes are to be seen.

Experiment 45. Operation performed September 8, 1905. Animal killed September 20, 1905. Fracture of twelve days' duration.

Macroscopic Description. The wound had healed by first intention, but at the upper end a stitch had broken and there was a clean, granulating area, covered with a scab. No pus was present. At the site of the operative wound no callus could be noticed, but at the ends, where the periosteum had been cut off, some thickening could be felt.

Longitudinal section through the bone revealed the fact that the sawcut had been made opposite to the entrance of the nutrient artery into the medullary cavity. The sawcut was filled flush with the surface of the old bone with yellowish-white, cancellous bone which extended into the lumen of the medullary canal 2 mm., but was not quite 4 mm. in length, extending equally above and below the sawcut. The nutrient artery gave off its large branch to the upper end of the bone directly opposite to this mass. The marrow was red excepting in the lowermost portion of the bone, where it was pink. Where the periosteum had been cut off, 9 mm. above the sawcut, there was a new formation of bone 1 mm. thick, extending upward 15 mm. There was no new bone formation from the lower portion.

Microscopic Description. The sawcut has entered the medullary cavity and has given rise to an abundance of osteoid

trabeculæ. This mass extends about half-way across the lumen of the medullary canal. It is composed of a network of osteoid trabeculæ with fairly large medullary spaces between, containing a lining layer of polygonal cells (osteoblasts) and, in the centre, loose connective tissue and engorged thin-walled bloodvessels. On the outskirts of the rounded mass of callus there is, in places, a layer of loose connective tissue and then red marrow containing greatly engorged bloodvessels. There are some osteoclasts to be seen in the medullary spaces between the trabeculæ. In a few of the dilated Haversian spaces of the cortex next to the medullary cavity there is hyperplasia of the endosteum, with osteoid trabeculæ formation where they have been cut across. The cortex shows great absorption, especially near the superficial portions of the bone and in the neighborhood of the sawcut; also a great number of osteoclasts. In areas the absorption extends well into the cortex, forming new, wide Haversian spaces, which connect with the new medullary spaces between the trabeculæ in the sawcut. On the periosteal surface there is an abundance of osteoid tissue at a distance from the sawcut where the periosteum had been cut off at the time of operation. The raised periosteum is hyperplastic in its deeper layers. The general trend of the trabeculæ is away from the sawcut. The explanation of this direction may be in the fact that the periosteum proliferates and forms trabeculæ, but does not grow in length, so that, when it is raised up, it swings as on a pivot and its end is opposite a relatively higher point on the bone, giving a diagonal direction to the trabeculæ. The cortex, from which the periosteum has been removed, exhibits some lacunar absorption, but it is not very marked, being from the body of the cortex outward and not originating on the surface. On the other side of the sawcut also, just in continuity with the tissue in the cut, are some osteoid trabeculæ. These do not appear to be periosteal in origin, because the general trend of the trabeculæ is toward the sawcut and not away from it. In addition the periosteum had been removed at the time of operation. Moreover, the trabeculæ are young, which would not be the case were they from the periosteum.

The superficial surface of the cortex on the side opposite to the sawcut shows lacunar absorption by osteoclasts and some proliferation of the deeper layers of the periosteum, but no new formation.

Experiment 46. Operation performed September 5, 1905. Animal killed September 20, 1905. Fracture of fifteen days' duration.

Macroscopic Description. The wound was entirely healed. On removal of the skin no callus but some slight thickening was found at the site of operation; also some tissue of a yellowish-white color.

The sawcut was filled flush with the surface by brownish-white, cancellous bone which extended into the medullary cavity and entirely occluded the lumen, extending 7 mm. longitudinally. Next to this, toward the lower ends of the bone, was a small area of a firm, whitish material, possibly cartilage, and then whitish marrow. The marrow of this bone does not appear to be congested. The periosteum was thickened where it had been cut off, but there were no signs of bone formation.

Microscopic Description. The periosteum, which was completely removed at operation, has not regenerated. The medullary cavity in the region of the sawcut is almost completely filled by osteoid trabeculæ, between which are large medullary spaces that are filled with loose connective tissue and numerous osteoclasts. The absorption of the trabeculæ is well under way. There is a very small amount of red marrow and some congested bloodvessels around the osteoid mass. The nutrient artery runs through the mass of osteoid tissue and demonstrates clearly that the adventitia of the bloodvessels takes no part in bone formation.

The sawcut is completely filled with osteoid trabeculæ, which do not appear to be very thick. The general direction of the trabeculæ is vertical to the line of the bone. There are some osteoclasts present, but not in such great abundance as in the medulla. The osteoid mass extends above the level of the bone and exhibits a tendency to "overflow" above and below the cut, as described in the previous specimens showing trabeculæ of endosteal origin on the periosteal aspect. There is little if any absorption of the cortex.

Experiment 47. Operation performed August 31, 1905. Animal killed September 19, 1905. Fracture of nineteen days' duration.

Macroscopic Description. The wound had healed by first intention. At the site of the bone wound nothing could be found, the bone apparently having entirely healed, leaving only a slight elevation at the site of operation.

On longitudinal section through the bone, practically no thickening was found on the periosteal side of the sawcut. The entire cut was filled flush with the surface by a brownish-white, cancellous bone which extended half-way across the lumen of the medullary canal. It was 10 mm. in length, with the greater part toward the upper end, following a branch of the nutrient artery. Next to the new bone there was a layer of a cartilaginous-looking material, and then red marrow. The principal branch of the nutrient artery going to the upper extremity of the bone runs through the callus.

Microscopic Description. Probably the periosteum had not been thoroughly removed a little to one side of the wound of the bone, as there is a small deposit of new bone at some distance from the sawcut which is distinctly localized. It is probably due to the leaving of the lower layer of the periosteum, as that membrane cannot be seen remaining in its

entirety. The lack of definite shape and direction of the trabeculæ confirm this conclusion.

The medullary cavity, in the region of the sawcut, is almost completely filled with osteoid tissue, the greater part of which is above the sawcut. Apparently, it is broken up into islands by branching bloodvessels, each island being surrounded by loose connective tissue or myxomatous tissue. The trabeculæ do not approach the vessels. Osteoclasts are present in moderate numbers. The sawcut is filled with osteoid trabeculæ, taking a vertical direction, extending above the level of the cut, and, as in the previous section, "overflowing" it on one side only, the direction of the trabeculæ being continuous with those in the sawcut (Fig. 20).

The bone itself shows little absorption, there being no communications between the medullary spaces of the osteoid tissue and the Haversian spaces. In the medulla, the whitish area noticed around the bone mass, is loose, myxomatous tissue surrounded by cellular red marrow.

Experiment 48. Operation performed August 22, 1905. Animal killed September 14, 1905. Fracture of twenty-three days' duration.

Macroscopic Description. The wound had healed by first intention. On removing the skin there was found a small amount of callus at the site of the operation

Longitudinal section through the bone demonstrated that the sawcut had been made opposite to and a little higher than the entrance of the nutrient artery into the medullary cavity. The sawcut was completely filled with a rather compact-looking bone which was slightly yellower in color than the old compact bone. On the periosteal side of the bone there was some soft, white material which appeared as if it might have contained cartilage, but did not look like typical callus. On the endosteal side of the sawcut there was a new formation of cancellous bone occluding one-half of the lumen of the medullary canal and extending 3 mm. above and 13 mm. below the sawcut in the direction the nutrient artery takes in the bone. Next to the bone there was a very thin layer of white, cartilaginous-looking material, and then congested marrow.

Microscopic Description. The sawcut has entered the medullary cavity and the medullary osteoid tissue is mostly in one direction from the sawcut. The osteoid tissue is more or less divided into masses with myxomatous tissue and red marrow on the edges. There are some osteoclasts present, but not in great abundance, and there is not much absorption of the internal callus. The sawcut is filled with osteoid tissue which is rather compact, but the direction of the medullary spaces is more transverse than usual. Near the periosteal aspect there is great absorption of the cortex, which blends with the new osteoid tissue, uniting the medullary spaces of the old and the new tissue (Fig. 21). Osteoclasts and osteoblasts are present in these spaces. There is osteoid bone formation in the periosteum, where it still remains attached.

Experiment 49. Operation performed July 6, 1905. Animal killed August 3, 1905. Fracture of twenty-eight days' duration.

Macroscopic Description. There were almost no signs of the operation, only a narrow, white, linear scar at the site of the operative wound. Feeling through the scar, there was at the site of the bone wound a slight depression with a small elevation on each side. After removal of the skin the bone was found to be recovered by a thin, filmy membrane, reënforced at the site of the operation by a thick, tough material. The cut was almost completely filled in, although evidence of it was still present.

On longitudinal section almost the entire medullary cavity of the bone was found to be filled by a firm callus, appearing as if it contained osteoid trabeculæ. The callus toward the lower extremity of the bone originated from that in the neighborhood of the sawcut and had grown into the medulla, for it was not attached to the endosteum at the sides, but appeared to be surrounded by dark-brown marrow. A rather large collection of marrow was found between the two portions, which connected with each other.

Microscopic Description. The ground specimen shows that the sawcut had entered the medullary cavity at one point, but not very deeply. Almost the entire cavity is filled with osteoid trabeculæ in separate batches or islands. They show some absorption, but not a very great amount. Some osteoclasts are present. Surrounding these masses is filamentous tissue containing some marrow cells. The sawcut is filled with osteoid trabeculæ which are continuous, with a considerable proliferation on the periosteal aspect, the origin of which it is impossible to determine. The trabeculæ fill in the sawcut on the sides, but not completely in the centre of the cut. The cortex shows widened spaces which communicate directly with the medullary spaces in the new trabeculæ. Osteoclasts are present in moderate numbers. Osteoblasts are abundant.

Among the osteoblasts and in the medullary spaces of the superficial portions of the callus there appears to be considerable hyaline material taking a diffuse eosin staining. It is present in the form of round masses or strands. What it is cannot be determined, but it looks as if it may be a homogeneous hyaline secretion from the osteoblasts.

Experiment 50. Operation performed August 17, 1905. Animal killed October 5, 1905. Fracture of forty-nine days' duration.

Macroscopic Description. The wound was found to have healed by first intention. There was considerable thickening of a somewhat cartilaginous nature directly over the sawcut, but it appeared to be somewhat movable; so that its nature could not be determined until section was made.

On longitudinal section through the bone, the periosteum was found to have apparently regenerated and was considerably thickened over the entire length of the specimen. The sawcut was entirely filled with whitish, hard bone, not so compact as the normal bone. The new bone extended about half-way across the medullary cavity and on each side of the sawcut for about 3 mm. Surrounding the new bone was red marrow and farther down yellow marrow.

Microscopic Description. The sections demonstrate that the gross description was in error, for there is no regrowth of the periosteum itself, but only of connective tissue. There is absolutely no new periosteal bone formation, but some lacunar absorption, making the superficial cortical surface rough.

In the medullary cavity there is a moderate amount of osteoid tissue which extends about half-way across the lumen of the canal. It is quite dense in structure, the medullary spaces being quite small and the trabeculæ thick. There is very little activity evident, there being no osteoblasts on the medullary trabeculæ and only a very moderate amount of osteoclasts, causing slow absorption of the endosteal callus. The medulla contains some marrow cells, but is not extremely cellular as in active states.

The sawcut is filled flush with the surface of the bone with osteoid tissue which is rather compact, but in which the general trend of the medullary spaces is becoming in the line of the bone instead of at right angles to it. There is distinct evidence of the former direction of the old trabeculæ in the streaks present in the new trabeculæ. Quite cellular, new, young bone fills in the sites of the old spaces. The new spaces are lined by osteoblasts and are directly continuous with the widened Haversian spaces of the old cortex (Fig. 32). They show a deposit of still younger new bone. The cortex is rarefied.

SERIES 5.

This series, for which dogs were used, was performed with the object of determining the activity of the bone itself when stripped of its periosteum and when not accompanied by visible injury to the medulla. Each operation consisted in making an incision over the tibia to the bone, reflecting the periosteum for about 2.5 cm., and then cutting off the reflected portion. In this denuded area of the cortex, one or two shallow sawcuts, not deep enough to enter the medullary cavity, were made. The wound was then sutured and the leg dressed as described under previous operations.

Experiment 51. Operation performed September 13, 1905. Animal killed September 16, 1905. Fracture of three days' duration.

Macroscopic Description. The dressing was full of blood and the wound still open. On removing the skin there was found a very large hematoma extending from the knee to the ankle. There was no infection. Longitudinal section showed the sawcut to be filled with blood. The medulla did not appear to be affected.

Microscopic Description. The sawcuts are filled with red blood corpuscles, a small amount of fibrin, and a few leukocytes. The periosteum has been stripped away and the surface of the cortex is smooth. There is little or no alteration of the medulla excepting, possibly, a slight increase in the congestion and free blood cells at the site of the canal immediately adjoining the cuts. This may have been produced by the fact that a vessel leaving the canal runs almost directly across the bone to the region of the cuts.

There are a few dilated spaces in the cortex containing osteoclasts and a lining of osteoblasts. These are found near the cuts in the bone, but also in other portions removed from the site of operation. The bone looks as if it had been the seat of recent activity because of an entirely distinct, rather thick layer of apparently new bone lining the medullary cavity. This formation has nothing to do with the operation performed for these experiments.

Experiment 52. Operation performed June 20, 1905. Animal killed June 25, 1905. Fracture of five days' duration.

Macroscopic Description. The wound was perfectly clean, healing progressing by first intention. There were some signs of organizing blood clot on the inner aspect of the bone. In the sawcut there was very little evidence of an effort on the part of nature to throw out callus. The sawcut contained some blood clot which was not disturbed.

Microscopic Description. The sections did not enter the medullary cavity, so its description must be omitted. The sawcut appears to be filled with red blood corpuscles and a small amount of fibrin. There are no evidences of the periosteum. There is no roughening or absorption of the superficial aspect of the cortex, or of the sides of the sawcut. The cortex shows possibly slight widening of the Haversian spaces, but to no great extent. There is no lacunal absorption to be noted and no osteoclasts are present. The tissue surrounding the bloodvessels in the Haversian canals exhibits some proliferation, but not sufficient to form a layer of osteoblasts.

Experiment 53. Operation performed September 12, 1905. Animal killed September 24, 1905. Fracture of twelve days' duration.

Macroscopic Description. The wound was found to have healed at all points excepting the upper extremity, which had pulled apart and was healing by granulations. At the site of the bone wound everything was covered with connective tissue, so that nothing definite could be distinguished.

Longitudinal section through the bone showed the sawcut to have been made opposite to and 3 mm. above the point of entrance of the nutrient artery into the medullary cavity. In the section made the sawcut did not appear to have

entered the medulla, but the medullary cavity in the region of the cut contained new bone or osteoid tissue 1.5 mm. thick and 10 mm. long in the direction of the nutrient artery. The medulla was red. The sawcut was filled with a somewhat reddish material, but no bone. The periosteum, 5 mm. above the sawcut, was 2 mm. thick and appeared to contain cartilage; below it did not. It appeared as if the periosteum had regrown over the sawcut.

Microscopic Description. The entire cortex is absolutely riddled with very wide Haversian spaces, which show, in some places, very large numbers of osteoclasts, one small space containing eleven of them. All these dilated spaces contain an abundance of loose myxomatous tissue in addition to bloodvessels, some marrow cells, and a layer of osteoblasts. The sawcut is absorbed to so great an extent that it can hardly be recognized as a straight cut. Spicules of bone around a depression show where it had been made. While in none of the sections has it penetrated the medullary canal, it has approached very close to it and has cut across a couple of Haversian canals, which go directly into the canal from the cut, forming narrow communications between the two.

The periosteum contains a fair amount of osteoid tissue at a distance from the wound and a thin, irregular layer up to the edge of the cut. The sawcut also contains some trabeculæ which do not stream upward as in other series, but form large, round canals lined with osteoblasts and connective tissue. Whether these trabeculæ and the thin layer on the periosteal surface arise from cells of the deeper layer of the periosteum inadvertently left remaining, or are from the Haversian canals of the bone, it is impossible to determine.

The irritation has extended also into the medulla by referred stimulus along the communicating Haversian spaces. There is a nodule of osteoid trabeculæ in the medullary canal opposite to the sawcut. It differs from previous endosteal growths in not being irregular, but distinctly limited by a membrane resembling the deeper layer of the periosteum (endosteum) (Fig. 24). The medulla is red and cellular, but does not show web-like formation of connective tissue.

Experiment 54. Operation performed August 29, 1905. Animal killed September 22, 1905. Fracture of twenty-four days' duration.

Macroscopic Description. The wound had healed perfectly. There was no pus present. There was no callus formation, but some thickening at the ends of the periosteum where it had been cut off. The sawcut was still plainly visible and not completely filled in except by a reddish material.

Longitudinal section revealed the fact that the sawcut was very shallow and had been made 5 mm. lower down than the entrance of the nutrient artery into the medullary canal. The medulla was not apparently affected by it. The cut was filled with white and brown material, not very firm in consistence. Where the periosteum had been cut off 10 mm. below the sawcut, there was a very thin formation of new white bone not 1 mm. in thickness and extending for about 10 mm. down the bone. There was a suggestion of the same thing at the upper end. The bone-marrow was red in the upper three-fifths and yellow below.

Microscopic Description. The sawcut is rather shallow. The periosteum, where it had been left remaining, shows the formation of a layer of osteoid trabeculæ of fair size. There are no signs of periosteum over the portion where it had been removed at the operation, and there is no superficial lacunar absorption. The sawcut is filled with young fibroblasts and bloodvessels, *i. e.*, granulation tissue with some slight traces of the original blood clot remaining.

There is very marked absorption of the cortex, with very large dilated Haversian spaces containing osteoclasts, a lining membrane of osteoblasts, loose connective tissue of myxomatous nature, and bloodvessels. The medulla is of the red, cellular variety. On the medullary aspect of the cortex, at the site of the saw wound, is a small, flat elevation or nodule of newly formed osteoid trabeculæ (Fig. 23), lined with polygonal osteoblasts, around which is a thin layer of connective tissue. Outside of this is red marrow. There are no osteoid trabeculæ in the marrow detached from the endosteum, demonstrating clearly that the endosteum has been stimulated to growth by the injury to the bone above.

Experiment 55. Operation performed July 3, 1905. Animal killed August 2, 1905. Fracture of thirty days' duration.

Macroscopic Description. The wound had healed by first intention. There was no callus visible, but the periosteum (?) had again apparently covered the bone and was continuous over the wound in the bone as a thin, film-like membrane.

Microscopic Description. The sawcut has not penetrated into the medullary cavity. There is no periosteal new bone formation or absorption, the surface being smooth. There is a fibrous tissue covering the bone, but whether it is periosteum or not it is impossible to state. The sawcut is filled with cellular, fibrous tissue like granulation tissue. Some of the deeper cells are very large, with oval, vesicular nuclei. One side of the sawcut shows marked lacunar absorption apparently by osteoclasts. A small portion of the wound looks as if there is a beginning deposition of new bone lined with a layer of osteoblasts. Their origin is unknown, but it is doubtful if it is periosteal, because the periosteum exhibits no signs of activity elsewhere. There is a tendency to the formation of cancellous tissue on the medullary aspect of the cortex, there being large spaces filled with cellular marrow.

The medulla is red and cellular only in the neighborhood of the sawcut. There is no apparent new bone formation. There is only a very moderate amount of absorption of the cortex.

Experiment 56. Operation performed August 18, 1905. Animal killed September 22, 1905. Fracture of thirty-five days' duration.

Macroscopic Description. The wound had healed by first intention. On removing the skin there was found practically no effort at repair, no callus being present. The sawcut was perfectly visible.

Longitudinal section through the bone demonstrated that the sawcut had been made opposite to and 10 mm. farther up on the bone than the entrance of the nutrient artery into the medullary cavity. The medullary cavity was not at all changed, but the marrow was red. The sawcut did not enter the medulla. The periosteum had apparently regrown over the portion where it had been denuded and filled in the sawcut, but there was no attempt at callus formation.

Microscopic Description. The sawcut is shallow, not penetrating far into the cortex. There is a formation of osteoid trabeculæ in the periosteum, where it still remains attached at some distance from the sawcut. There are no trabeculæ near the sawcut. The cut is filled in, apparently with granulation tissue. There is absorption of the sides of the cut.

The cortex shows great absorption with widened Haversian spaces lined by osteoclasts. The marrow is red and cellular. On the medullary side of the cortex, in the region of the sawcut, there is a small deposit of newly formed osteoid trabeculæ. The marrow exhibits no connective-tissue hyperplasia in that region.

Experiment 57. Operation performed June 20, 1905. Animal killed August 4, 1905. Fracture of forty-five days' duration.

Macroscopic Description. There was superficial sloughing of the tissues on the outer aspect of the thigh. The wound itself was unaffected. At the site of fracture, on removal of the skin, there was found no evidence of the sawcut, but the area was covered with a cartilaginous material which was probably callus from regenerated periosteum.

On section through the bone there was no evidence of the sawcut excepting a narrow, dark spot on the upper end, in the cancellous portion.

Microscopic Description. The sawcut has not entered the medullary cavity. The periosteum contains some new bone formation at a distance from the wound, but none near it. The sawcut is filled by osteoid trabeculæ having a transverse direction of the spaces between them. There are evidences that the original direction was in the line of the cut. The cortex has undergone great absorption, especially between the bottom of the sawcut and the medulla (Fig. 25). The spaces are very wide and form communications between the cut and the medullary side of the bone. The medullary cavity contains a considerable amount of osteoid tissue in the region of the sawcut. As shown by the ground specimen, this tissue has large medullary spaces. The medulla is red.

Experiment 58. Operation performed August 17, 1905. Animal killed October 26, 1905. Fracture of seventy days' duration.

Macroscopic Description. The wound was found to have healed by first intention. The bone was completely covered by tissue, which was probably periosteum. At one point, doubtless the site of operation, there was a moderate elevation quite hard in consistency, which may have been callus or bone.

Section in a longitudinal direction showed practically no signs of the operation on the bone, which was performed opposite to the entrance of the nutrient artery into the medullary cavity. The sawcut was entirely filled with hard tissue. There was no apparent new bone formation on the endosteal side, but there was a layer of red marrow 1.5 mm. thick on the side of the sawcut, beyond which was yellow marrow.

Microscopic Description. The sawcut is completely filled, flush with the surface of the bone, by new compact bone which has fewer medullary spaces than the surrounding cortex (Fig. 26). There was probably an excess, which has been removed, as the periosteal aspect of the new bone shows osteoclastic lacunar absorption (Fig. 27), as does the surface of the cortex. The medullary spaces of the new bone have a tendency to communicate with those of the cortex. The cortex has undergone considerable absorption, the dilated spaces often containing fat and medullary cells, but no osteoblasts as distinct cell layers. Osteoclasts are not found in the cortex. The cortex, under the periosteum where it still remains, distant from the cut, exhibits considerable osteoclastic absorption. There is a new bone formation of moderate size in the medullary cavity against the inner side of the cortex in the region of the sawcut. It has suffered considerable osteoclastic absorption. The medulla is cellular, but not to the extent of obliterating the fat cells.

SERIES 6.

This series, upon dogs, was performed with the object of determining the activity of the periosteum, when raised from the bone and accompanied by injury to the bone not deep enough to penetrate the medullary cavity. Each operation consisted in making an incision over the tibia to the bone, and then, in most cases, raising the periosteum from the bone by making an incision in the line of the bone and passing a periosteal elevator under the membrane. After raising the periosteum, a saw was passed under it and a couple of very shallow sawcuts made in the bone, and the periosteum again allowed to fall back into place. In a couple of instances the periosteum was cut across, and after

making the injury to the bone was sutured in place by catgut. Before closing the wound the periosteum was tapped sharply several times with some blunt instrument to cause more injury. The wound was then sutured with silk and covered with collodion.

Experiment 59. Operation performed February 19, 1906. Animal killed February 21, 1906. Fracture of two days' duration.

Macroscopic Description. The wound was found to be clean, with the sutures and collodion still in place. On removing the skin at the site of the operation, the periosteum was seen to be raised up and thickened and was of a reddish appearance, as if it consisted of organized blood clot. It was quite firm in consistency and extended beyond the confines of the bone.

Longitudinal section through the bone confirmed the findings before ection. The medulla was pink in color. There were no changes in the medullary cavity.

Microscopic Description. There is a large amount of blood clot with fibrin and an abundance of polymorphonuclear leukocytes. Under the raised periosteum are several areas of hyaline, fibrillar material, showing a small amount of leukocytic infiltration. The bone is not altered; the medulla is slightly increased in cellular content, but is not red, cellular marrow. Some of the new cells are fairly large.

Experiment 60. Operation performed February 21, 1906. Animal killed February 24, 1906. Fracture of three days' duration.

Macroscopic Description. The wound was found to be perfectly clean, but not completely united, as the edges could be pulled apart with the escape of a small amount of serum. On removing the skin, the periosteum, at the site of the operation, appeared to be thickened, red and edematous, and did not appear to be attached to the underlying bone. The sawcuts could be distinctly felt.

Longitudinal section through the bone showed the periosteum to be thickened, but there was no alteration in the bone. The medulla was red.

Microscopic Description. The sawcuts are very shallow and are covered over by periosteum, which remains as a fibrous strip across the top. The cuts themselves are filled with blood clot (red blood corpuscles, fibrin, and leukocytes). The connective tissue outside the periosteum exhibits an abundant formation of young fibroblasts, which resemble closely portions of the deeper layer of the periosteum.

The periosteum itself, where it has been raised, remains as a distinct fibrous layer with no proliferation. Where it has remained attached to the bone, there is proliferation of both the superficial fibrous layer and of the deeper osteogenetic layer. The appearance of this deeper layer is rather odd. The cells gradually become larger as one goes deeper, until they appear to resemble large marrow cells, being loose in their disposition and not made polygonal by mutual compression. Several Haversian spaces, lined with similar cells, communicate with this layer of the periosteum. At one place there is just the beginning of the formation of bone. The superficial layers of the old bone cells appear somewhat larger and more vesicular-looking than the remainder. Some seem to be breaking loose and entering the periosteal tissue.

There is widening of the Haversian spaces of the cortex. These spaces contain abundant cellular tissue resembling marrow cells, which are showing a tendency to form layers around the sides. The nuclei of the bone cells around these spaces appear larger and more vesicular than those farther removed. Osteoclasts are present.

The medulla is very cellular. It contains cells of varying sizes, some small round cells with deeply staining, single nuclei (occasionally eccentrically placed); others, cells of the same nature, but larger and with more protoplasm; still others, with larger vesicular nuclei, and, finally, very large cells with a great abundance of protoplasm and four to ten rather large and vesicular nuclei. These cells are probably forming osteoclasts, derived from the last of the above-named cells. Haversian spaces connecting with the medullary cavity show the medullary cells streaming into them.

Experiment 61 Operation performed October 20, 1905. Animal killed October 24, 1905. Fracture of four days' duration.

Macroscopic Description. The wound was found to have healed by first intention. At the site of the operation there was a great amount of blood.

On section through the bone a blood clot was found under the periosteum at the site of the operation. The medulla was red but there was no evidence of proliferation.

Microscopic Description. The periosteum cannot be made out definitely as a distinct layer, but there are numerous thick bands of fibrous tissue to be seen. There is no proliferation present, but sections of the catgut probably identify these bands as periosteum. There is no roughening of the periosteal aspect of the cortex excepting where the periosteum is still attached. There is no new trabeculæ formation anywhere excepting on the side opposite to where the operation was performed. Here there is slight periosteal proliferation. The sawcut and all the tissues on the periosteal aspect are filled with blood.

The cortex of the entire bone shows great rarefaction, but few osteoclasts. These spaces are filled with an abundance of round or oval cells resembling marrow or liberated bone cells, also dilated bloodvessels. The medulla is red, containing many free red blood corpuscles. Fat is also present. There are, in addition, numerous round or oval cells, varying in size, with small or moderate-sized, round, well-staining nuclei. Especially toward the ends of the bone, some of these cells exhibit a slight increase of the protoplasm, but, what is more

noteworthy, is an apparent division of the nuclei into two or four parts. They appear as if they may be a forerunner of the osteoclasts a few of which are to be found in the medulla.

Experiment 62. Operation performed February 16, 1906. Animal killed February 24, 1906. Fracture of eight days' duration.

Macroscopic Description. The wound had healed by first intention. On removing the skin the periosteum was found to have been raised up and thickened and was reddish white in color. A small amount of pink serum escaped when the skin was removed. Some irregularities could be felt on the bone surface.

Longitudinal section through the bone showed great thickening of the periosteum, with no apparent callus or new bone formation. The marrow was reddish in color. The bone seemed rather porous.

Microscopic Description. The periosteum was present as a distinct continuous layer, fibrous tissue above and markedly proliferated cells below. The osteogenetic layer, for the entire length of the bone, exhibits considerable cellular proliferation, which dips down into the saweuts. One cut contains blood and fibrin, being displaced by an ingrowth of this tissue. There are osteoid trabeculæ in the periosteal tissue up near one of the saweuts, and a beginning formation of them can be found in the bottom of it. There is great absorption of the entire cortex by osteoclasts. Cells are arranging themselves in layers along the sides of the widened canals. The medulla is red and contains many very large multinuclear cells (osteoclasts). There is a formation of osteoid trabeculæ on the medullary aspect of the cortex on the side of and in the region of the saweut.

Experiment 63. Operation performed February 23, 1906. Animal killed March 5, 1906. Fracture of ten days' duration.

Macroscopic Description. The wound had not closed, the stitches having been torn out. It was healing by granulation. There was no pus visible and there was no apparent change in the bone even after removing the skin.

On longitudinal section, slight thickening of the periosteum was found at the site of the operation, but there was no apparent callus to be seen. The medulla was not affected.

Microscopic Description. Owing to the fact that it was practically a compound fracture, there is such an abundance of young fibrous tissue that it is difficult to distinguish periosteal tissue from the remainder. However, there is tissue denser in some places than others, forming a layer which is probably the fibrous portion of the periosteum. Beneath it there is an abundance of young fibrous tissue or osteogenetic tissue, its exact nature not being determinable owing to the fact that the cells are more closely packed and not quite so large as is usual with osteoblasts. In addition, there are present more bloodvessels than is usual.

In areas there is lacunar absorption of the superficial portions of the cortex. There are some areas that resemble typical portions of the proliferated osteogenetic layer of the periosteum. At the base of one of the cuts and in a couple of additional areas, there is just the beginning formation of trabeculæ. The cortex proper contains an abundance of osteoclasts and a few large spaces caused by lacunar absorption. Some of these connect with the periosteum. They are lined by osteoclasts. The medulla is red and congested, but many fat cells remain. It shows a moderate amount of osteoclasts. On the endosteal surface of the cortex is a layer of cells resembling osteoblasts, but no endosteal trabeculæ.

Experiment 64. Operation performed March 2, 1906. Animal killed March 16, 1906. Fracture of fourteen days' duration.

Macroscopic Description. The wound had united perfectly excepting over the upper portion, where there was a granulating area, but no pus present. This area did not appear to communicate with the bone. On removal of the skin there was found a slight elevation at the site of the operation on the bone, but no callus was apparent.

On longitudinal section of the bone, slight thickening of the tissues over the site of the operation on the bone was found, but no callus. The bone was very small and the medullary cavity very narrow. The medulla was quite red throughout its entire extent.

Microscopic Description. The periosteum is present as a distinct layer and the saweuts are very shallow. The deeper layer of the periosteum is proliferated and fills in the saweuts with osteoblasts. There is a new osteoid bone formation from the periosteum extending up to the edge of the saweuts. Its trabeculæ are covered with osteoblasts. In areas where there are no trabeculæ there is lacunar absorption of the surface of the cortex. These areas are covered by a layer of large cells, with large, oval, vesicular nuclei. There are a few osteoclasts to be seen. Absorption is evident in the saweuts. There is practically no absorption of the cortex itself and its spaces do not appear to be lined by osteoclasts.

The medulla shows only a slight increase in its cellular content. It is most marked near the medullary border of the cortex, where there are some large cells with single, large, round, vesicular nuclei. No osteoblasts can be seen in the medulla.

Experiment 65. Operation performed February 2, 1906. Animal killed February 21, 1906. Fracture of nineteen days' duration.

Macroscopic Description. The wound had healed perfectly. At the site of the operation there was a marked nodulation, fairly firm in consistency, and not entirely adherent to the scar. Through some error, on removing the skin this nodule was cut across. It was fairly firm, but looked

more like granulation tissue than cartilage. The bone was still bare, the periosteum not being adherent to it. The sawcuts were plainly visible. The entire portion of the periosteum, that had been raised, was considerably thickened.

Longitudinal section showed the periosteum to be thickened and not adherent to the injured bone. Toward the lower end of the bone, where the periosteum was still attached, there was a small area of periosteal new bone formation about 1 cm. in length and 1 mm. thick. There was a thin layer of new cancellous bone in the medullary cavity opposite to the site of the operation.

Microscopic Description. The periosteum is raised up and not attached to the bone except at the ends where it had been left at the operation. At both of these situations there is a large formation of osteoid tissue. Its trabeculæ are covered with osteoblasts and also numerous osteoclasts. Where the periosteum had been raised up, it is greatly thickened and contains abundant fibroblasts, that is, large spindle cells with oval, vesicular nuclei. These are not arranged in a single layer, all going in the same direction, but appear to course in all directions. Some of the cells are especially large and, in one area, there appears to be an attempt at trabeculæ formation which is not, however, impregnated with calcareous salts, but merely hyaline in appearance. There is a moderate leukocytic infiltration present.

Some portions of the superficial aspect of the cortex have undergone absorption. The sawcuts show no absorption. There is moderate absorption of the cortex proper, its spaces being lined with osteoblasts.

In the medulla there is a rather large growth of osteoid trabeculæ, covered with large osteoblasts. No osteoclasts can be noted among the trabeculæ or in the marrow itself. The marrow is more cellular than normal, but not very red. There is connective-tissue hyperplasia of the marrow in the region of the osteoid tissue.

Experiment 66. Operation performed January 26, 1906. Animal killed February 24, 1906. Fracture of twenty-nine days' duration.

Macroscopic Description. The wound had healed by first intention. The scar was not adherent to the underlying tissue. Examination revealed an apparent thickening on the bone at the site of the operation and a small nodule, somewhat movable, on the anterior aspect of the bone, probably at the site of a catgut suture. On removal of the skin the inequalities of the surface of the bone could no longer be detected. The thickening was not appreciable to the naked eye. The small nodule mentioned was soft and yellowish in color.

Longitudinal section through the bone showed thickening of the periosteum at the site of the operation. The cuts were no longer visible in the bone, but there was present what was possibly a very thin layer of cartilage. The bone was a little thicker at the site of the operation, but it was impossible to say if there was new bone present. The medulla was reddish in color.

Microscopic Description. The periosteum is apparent as a distinct layer, but mostly fibrous in nature. There is not much activity present, it having already ceased. There is an abundance of periosteal osteoid trabeculæ above and below the site of operation, and less at the operative wound. The principal activity to be seen now is great absorption on the surface of the newly formed trabeculæ and the formation of wide, longitudinal Haversian canals in its deeper layers. Large osteoclasts are present in great abundance, and also a thin layer of apparently inactive osteoblasts. The spaces in the periosteal trabeculæ, as well as in the cortex, are filled with myxomatous tissue, in greater part, in addition to some marrow cells and a thin layer of osteoblasts.

The cortex on its surface, sawcuts, and body, exhibits great absorption being riddled with osteoclasts and having its spaces filled in as stated above. Its canals communicate freely with those of the periosteal trabeculæ. In the medullary cavity there are the remains of osteoid trabeculæ which show considerable absorption. Osteoblasts are no longer present. The marrow is red on the edges and yellow in the centre. There are osteoclasts in its substance.

Experiment 67. Operation performed January 26, 1906. Animal killed March 5, 1906. Fracture of thirty-eight days' duration.

Macroscopic Description. The wound had healed by first intention. Palpation revealed some roughening at the site of the operation, with two especially hard and nodular places, giving the impression that the catgut had failed to absorb. On removing the skin the tissues and the two nodules mentioned above were found to be freely movable over the bone.

Longitudinal section through the bone showed some thickening over the site of the injury to the bone, but there was no apparent callus. The medulla did not appear to be affected.

Microscopic Description. The periosteum exhibits some proliferation of its deeper layer. The injury to the bone is filled with young osteoid trabeculæ which have wide medullary spaces and are covered with osteoblasts. Their general direction is indefinite, but more in the direction of the bone than otherwise. The tissue in the spaces is of a loose cellular type, but not myxomatous in appearance. There is no absorption of the trabeculæ.

Beyond where the periosteum was sewed together there is a thin layer of compact new bone. The direction of the spaces in it are not oblique as in other instances, but more longitudinal. The catgut is present and encapsulated with fibroblasts. There is superficial absorption of the cortex by osteoclasts. The cortex proper shows very slight absorption, all of which is in the neighborhood of the periosteum. Its

canals contain some osteoclasts, marrow cells, and doubtful osteoblasts. A few of the canals communicate with the spaces of the new bone formation. The medulla is cellular at the edges and yellow at the centre. There are no osteoid trabeculæ in the medullary cavity. The marrow contains some osteoclasts.

Experiment 68. Operation performed January 26, 1906. Animal killed March 16, 1906. Fracture of forty-nine days' duration.

Macroscopic Description. The wound had united by first intention. On palpation through the skin, a small nodule could be felt at the site of the operation upon the bone. On removal of the skin the nodule appeared to be attached to the bone. In addition, there was found what seemed to be an unabsorbed strand of catgut. There was very little callus found at the site of operation.

Longitudinal section through the bone showed slight thickening of the periosteum at the site of the operation, but no callus. The medulla, apparently, was not affected, being light pink in color.

Microscopic Description. The catgut is undergoing absorption by leukocytes and a few giant cells. The periosteum appears to be mostly fibrous in nature, having ceased most of its activity. The bone wound is filled in with quite compact osteoid tissue, the general direction of the trabeculæ being in the line of the bone. Its spaces communicate with the old Haversian spaces of the cortex. The trabeculæ are still covered with osteoblasts which do not appear to be very active. There is absorption of its superficial portions.

Excluding superficial absorption, the cortex shows practically no rarefaction, but looks as if it had undergone absorption in places, and had been refilled with new bone. This impression is given by the different shades of staining in the cortical bone.

The medullary cavity contains a great number of osteoid trabeculæ which are rather dense. They are covered with osteoblasts, but no absorption is apparent. The medulla is red near the trabeculæ and shows an increase in its connective tissue. It contains some osteoclasts.

(*To be continued.*)

BOOK REVIEWS.

Die Behandlung der Tuberkulosen Wirbelsaulen-entzundung. Von Dr. F. Calot. (The Treatment of Tubercular Disease of the Spine.) Translation in German by P. Ewald.

This is a German translation of Calot's recent work in French on the treatment of Pott's disease of the spine.

It is a small monograph, 90 pages, illustrated by 120 cuts and written in a wonderfully clear and concise style that lends itself admirably to translation. Calot says that reduction of the deformity in Pott's disease is not only permissible, but is necessary and positively indicated, exactly as is the correction of similar deformities in tuberculous hip and knee disease. The correction of the deformity is no longer attempted at a single sitting, but spread over five, ten, or fifteen.

The patient is to be extended by means of a tripod and head sling only to such a degree as can be obtained without taking either the toes or heel off the floor. An extensive plaster jacket is then to be applied which has windows cut over the hump and over the chest and abdomen. Every two months the window over the hump is opened and cotton compresses inserted; the window is then closed with a few turns of a plaster bandage, which is afterward cut away from the anterior window. In five or six months a new plaster bandage may be applied. A permanent ankylosis in a corrected position will be obtained usually inside of three years; sometimes it takes two or three years longer, often inside of two years. During the later stages of treatment a celluloid or leather jacket, made over a cast, is applied.

Abscesses are never opened, but may be tapped and injected with an iodoform or camphor mixture.

The book is a valuable contribution to the treatment of Pott's disease which will be particularly acceptable to those who wish to have Calot's views and methods expounded in the German language. G. G. D.

A Compend of Operative Gynecology. By William Seaman Bainbridge and Harold D. Meeker. New York: The Grafton Press.

This little book of 66 pages has been compiled from the lectures delivered by Dr. Bainbridge before the class in Operative Gynecology upon the Cadaver at the New York Post-Graduate Medical School.

The various operations upon the pelvic floor and upon the internal generative organs are clearly described with a pleasing attention to detail, the balance of the book being devoted to a consideration of the various forms of hernia, appendectomy, coccygectomy, and excision of the breast. While some of these subjects might well be considered as foreign to a compend upon gynecology, the exigencies of the work of the operating gynecologist render their inclusion a necessity.

The directions for the performance of the various operative procedures are concise, yet clear, and we note with pleasure the absence of any attempt to illustrate the book.

As an aid to the student in operative surgery upon the cadaver, we feel that the book will fill a want and that it is admirably adapted to its purpose.

W. R. N.

UNIVERSITY OF PENNSYLVANIA
DEPARTMENT OF MEDICINE

FOUNDED IN 1765

This Medical School, the oldest in the United States, was founded in 1765 by Dr. John Morgan, who filled in it the first medical professorship created in America. In his opening "Discourse upon the Institution of Medical Schools in America," delivered in the College of Philadelphia May 30, 1765, Dr. Morgan uttered these prophetic words: "Perhaps this medical institution, the first of its kind in America, though small in its beginning, may receive a constant increase of strength, and annually exert new vigor. It may collect a number of young persons, of more than ordinary abilities, and so improve their knowledge as to spread its reputation to distant parts. By sending these abroad duly qualified, or by exciting an emulation amongst men of parts and literature, it may give birth to other useful institutions of a similar nature, or occasional rise, by its example, to numerous societies of different kinds, calculated to spread the light of knowledge through the whole American continent, wherever inhabited."

Through Dr. Morgan, the pupil of Hunter in London and of Cullen in Edinburgh, the graduates of this school take a just pride in regarding it as the lineal descendant of the best medical schools of Great Britain in the last century. To Dr. Morgan was soon joined another pupil of Cullen, Dr. William Shippen, as Professor of Anatomy and Surgery, thus forming another tie of relationship to the celebrated University of Edinburgh, whose methods of instruction were substantially adopted here. In the next year Dr. Adam Kuhn was added as Professor of Botany and Materia Medica; and in June, 1768, a "Commencement was held," at which medical honors were bestowed, the first in point of time in America. In 1769, Dr. Benjamin Rush was elected Professor of Chemistry, while Dr. Thomas Bond, one of the trustees of the College of Philadelphia, delivered lectures on Clinical Medicine in the Pennsylvania Hospital.

To the faculty thus composed of Morgan, Shippen, Bond, Kuhn, and Rush, have succeeded, at various times, professors whose reputation has been national, such as Wistar, Barton, Physick, Chapman, Hare, Gibson Horner, Dewees, Jackson, George B. Wood, Hodge, James B. Rogers, Carson, R. E. Rogers, Leidy, Henry H. Smith, Pepper, Francis Gurney Smith, Stillé, D. Hayes Agnew, Goodell, W. Pepper, Jr., and Ashhurst.

ADMISSION.

Admission to the Department of Medicine may be obtained either: I, by diploma; or II, by examination; or in certain cases, as specified below under 1, by a combination of both methods.

I. Admission by Diploma: Any candidate who may have received a degree in Arts or Science from a college recognized by this University will be admitted without examination. Candidates who may have been admitted by examination to the two-year course in Biology of this University, and who may have satisfactorily completed the course, will be exempt from the entrance examination. Any candidate who may present written evidence of having passed the entrance examinations of a recognized college, in which the requirements are equivalent to those demanded for entrance to the Freshman Class of the College (Arts and Science Courses) of this University, will be admitted without examination.

Diplomas of public high schools may be accepted as complete or partial certificates. All diplomas presented by candidates will be referred to Faculty Committee No. 1 of the College Faculty (Academic), who will examine each case and decide whether the diplomas shall be accepted in lieu of examinations, and what subjects they properly cover. The diploma must be transmitted to the Dean of the Medical Faculty not later than June 10 or September 10 in each year, and must be accompanied by a certificate signed by the principal of the school, stating the exact amount of each subject covered by the diploma, and the mark or grade attained in each subject.

II. Admission by Examination: The required subjects of examination for entrance to the Department of Medicine are the same as those prescribed for admission to the Freshman Class of the College (Arts and Science Courses) of the University of Pennsylvania.

The course of instruction extends over four years, with one session, beginning the last Friday in September and ending on the third Wednesday in June in each year.

James Tyson, M.D., Professor of Medicine.

Horatio C. Wood, M.D., LL.D., Emeritus Professor of Materia Medica, Pharmacy, and General Therapeutics.

Edward T. Reichert, M.D., Professor of Physiology.

Barton Cooke Hirst, M.D., Professor of Obstetrics.

J. William White, M.D., John Rhea Barton Professor of Surgery.

George A. Piersol, M.D., Professor of Anatomy.

John Marshall, M.D., Nat.Sc.D., LL.D., Professor of Chemistry and Toxicology.

Louis A. Duhring, M.D., Professor of Dermatology.

Alexander C. Abbott, M.D., Pepper Professor of Hygiene and Bacteriology.

John G. Clark, M.D., Professor of Gynecology.

George E. de Schweinitz, M.D., Professor of Ophthalmology.

Charles H. Frazier, M.D., Professor of Clinical Surgery, and Dean of the Faculty.

Allen J. Smith, M.D., Professor of Pathology.

De Forest Willard, M.D., Professor of Orthopedic Surgery.

B. Alexander Randall, M.D., Clinical Professor of Diseases of the Ear.

J. P. Crozer Griffith, M.D., Clinical Professor of Diseases of Children.

John H. Musser, M.D., Professor of Clinical Medicine.

Alfred Stengel, M.D., Professor of Clinical Medicine.

Gwilym G. Davis, M.D., M.R.C.S. Eng., Associate Professor of Applied Anatomy.

Edward Martin, M.D., Professor of Clinical Surgery.

Thomas R. Neilson, M.D., Clinical Professor of Genito-Urinary Diseases.

Charles K. Mills, M.D., Professor of Neurology.

William G. Spiller, M.D., Professor of Neuropathology and Associate Professor of Neurology.

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UNIVERSITY OF PENNSYLVANIA MEDICAL BULLETIN.

AN INVESTIGATION OF THE PHYSICAL, CHEMICAL, AND BIOLOGICAL CONDITION OF THE AIR IN THE PHILADELPHIA RAPID TRANSIT SUBWAY.

By Hervey L. Bates, M.D.,
Thomas A. Scott Fellow in Hygiene, Laboratory of Hygiene, University of Pennsylvania, 1906–1907.

(From the Laboratory of Hygiene, University of Pennsylvania.)

"Mountains interposed make enemies of nations." To reach the plains of Marengo a century ago, Napoleon immortalized himself by his daring passage of the Alps. The glory of this feat was only equalled by the overwhelming victory which followed.

Fifty years later an unworthy namesake of the Great Napoleon sent another army over the Alps to restore to Pius IX his papal tiara, utterly defeating the Republican movement under Garibaldi.

It was during this latter exciting period of European history that French and Italian scientists and engineers conceived the stupendous project of tunnelling Mont Cenis, an Alpine peak, separating Bardouneche on the Italian side from the little French town of Tourneaux. Thus, while Magenta and Solferino are being fought overhead, we find science digging a little hole through the Alps, which was destined to be worth many millions more to the peace of France and Italy than the many millions required to dig it. When something over fourteen millions of dollars had been expended and nearly twelve hundred human lives had been sacrificed, the diggers from each end met in the middle and celebrated the completion of the first great modern triumph in underground railroad construction. It is interesting to note a similar celebration which occurred two thousand years before Napoleon was born. It was during the reign of King Hezekiah that the aqueduct tunnel of Siloah near Jerusalem was completed, and the meeting of the diggers commemorated by an inscription which was recently discovered by certain Eastern excavators. The tunnel dug in ancient Babylon under the Euphrates River was probably five centuries old when King Hezekiah reigned in Jerusalem, and is certainly the earliest under-water tunnel of which there is any record. The Romans were well versed in the art of tunnel construction. Excavations in 1873 disclosed a tunnel three miles long, with an average height of thirty feet, bearing the date of the Emperor Claudius. In Egypt, also, we find the tunnel; those beneath the great Pyramids dating back at least five thousand years. Thus, we are able to trace the modern municipal subway to an origin in remote antiquity.

Since the completion of the Mont Cenis Tunnel several others have pierced the Alps, some of very considerable length (Tauerntunnel, 8526 meters; Karawanken, 7976 meters).[1] One of the oldest and longest railroad tunnels in this country is the Hoosac Tunnel, in Massachusetts. It is nearly five miles long.

Of course, the question of ventilation in an underground structure of this size is of paramount importance from the very start. The use of belt-conveyors[2] and other mechanical devices in excavating has considerably reduced the number of men required to do the work; but this few must be constantly supplied with fresh air. Once the tunnel is completed, the problem is much simplified by the comparatively short time spent in passing through, but there is, as has been demonstrated more than once, always the possibility of a train's breaking down in the middle of the tunnel. The systems at present in use are all more or less unsatisfactory.[1]

Coming to the question of subway ventilation, we find a much easier problem, owing to the possibility of having air-shafts to the surface, which, of course, is eminently impossible in a mountain tunnel. In London, in 1895, there were several "tubes," operated by steam and lighted by gas, only one of which was at that time artificially ventilated. In the Mersey Tunnel (four miles long, operated by steam and lighted by gas), which had artificial ventilation, the air was said to be "reasonably good"(!).[3] This in spite of the fact that one New York elevated locomotive vitiates the air as much as twenty-five thousand people, while an ordinary locomotive is equivalent to eighty-seven thousand people.[3] The system of ventilation used in the Mersey Tunnel and later installed on the Great Northern and City Railways, London, simply consisted of a series of air-shafts with exhaust fans to maintain a current of air through them. John Featherstone, writing on "London Subways," and referring especially to those not having the air-shafts, says, "The cars fit the tunnel so closely as to pump air fairly satisfactorily." There was also in these tunnels a "large mine fan" which "sucked in fresh air" at night when the trains stopped. Of course, the use of electricity for motive power and illumination still further simplifies the problem. Prof. Homer S. Woodbridge, in his report to the Boston Transit Commission, says that thirty times as much ventilation is required if steam is used.

In producing air-currents in subway ventilation, the effect

on the direction in which the smoke would go in case of fire must be taken into consideration. If, for example, the smoke from a burning train followed the escaping passengers toward the nearest station, it would greatly increase the danger. For this reason, as well as to maintain the freshest air at the stations where the passengers spend most of their time, Mr. Rice's plan in New York is to exhaust the air midway between the stations. This is also the best way to carry dust. The air-shafts in the New York Subway are fitted with "louvers" (simple mechanical devices which permit the passage of a current of air in one direction only). At first it was thought that the movement of cars by piston and suction action, forcing air out through the ventilators and sucking fresh air in through the stations, would provide sufficient ventilation,[5] but it has been found necessary to combine this system with the more reliable electric fan.

In the Boston Subway, also, the fresh air is sucked in through the stations, the only objection to the system being the strong drafts which it causes on the station platforms. After four months' operation of the first five sections of the Boston Subway the general atmospheric conditions were pronounced satisfactory.[6] "From the short experience of the past four months," the same writer continues, "it does not appear that fans are essential for keeping the air pure and wholesome during the autumn and winter seasons, though when the subway is in full use they may sometimes be needed. It is, however, in the hot days of summer that fans may be imperative for the proper equalization of the temperature."

This brings up the subject of temperature in general, which, while in the nature of a digression, may properly be discussed at this point. Returning to the New York report,[5] we find the question of heat removal considered of "more importance than change of air."

According to this writer, 83 per cent. of the energy from the power-house appears as heat. Some of this is lost in the tunnel by radiation and conduction through the walls. Some by the same means and by convection currents reaches the stations and is there dispelled. But a sufficient amount remains to increase the temperature from 12° to 20° (!) in the absence of ventilation. If it becomes necessary, the excessive heat will be removed by refrigeration, rapid evaporation of water, or simply by the presence of water in the tunnel.

In marked contrast to the conditions in New York, we find in Boston[6] an actually lower temperature in the subway than outside, even in very hot weather. The following figures are quoted from the Boston Transit Commission's report for 1898: June 25, outside temperature = 82° F.; inside temperature = 66° F.; difference = 16° F. July 1, outside temperature = 82° F.; inside temperature = 66° F.; difference = 16° F. July 6, outside temperature = 87° F.; inside temperature = 69° F.; difference = 18° F. It is necessary to explain, however, that the above observations were made before the cars started running, the air, of course, being more or less stagnant; so that the differences are presumably in excess of what they would be under normal conditions.

Our observations of temperature in the Philadelphia Rapid Transit Subway cover a period of five months, from the latter part of January, 1907, to the latter part of June of the same year, thus covering three of the seasons—winter, spring, and summer. We used an ordinary Centigrade thermometer, exposing it for at least five minutes before each reading. Observations were made daily at Fifteenth and Nineteenth Streets Stations in the subway and at a point about half a square from Fifteenth and Market Streets outside the Subway, at which point most of the comparative outside observations of all kinds were made.

We found an average difference of about 3°. In cold weather (up to about 10°) the inside temperature was from 0.1° to 9° higher than the outside; while in warm weather the reverse held true except that the difference never amounted to more than 5.4°. As a rule, the difference was more marked on clear than on cloudy days, probably due to the fact that the presence of clouds prevented, to a certain extent, sudden changes in the outside temperature. In any case the rate of change is slower inside than out; for example, on May 8th (see Table I) we find the outside temperature 17.7°; inside, 16°. On May 9th the outside temperature suddenly drops to 12.8°, while the inside temperature, changing more slowly, only falls to 14.2°, leaving it actually higher than the outside temperature. Again, on May 16th and 17th, and on May 23d and 24th the same thing occurred.

The graphic chart (Chart I) is made by averaging three successive observations, on different days, thus avoiding sudden and temporary variations, and showing in a general way what we have just explained. It will be noted that until March 19th the average inside temperature was higher. During the warm weather in the latter part of March and early in April, the solid line, indicating outside temperature, is uppermost. A period of cold weather again changes the relation, and so it varies back and forth with the unusual changes of a very backward spring, both lines gradually rising, however, toward summer temperature, with the solid line showing a decided tendency to remain uppermost.

Returning to the subject of ventilation proper, we will consider in detail the system at present in use in the Market Street Subway. The Subway is now, and has been since the beginning of our observations, completed from Fifteenth Street Station to the Schuylkill River, a distance of about four thousand feet. Leaving out of consideration the stations, the tunnel has an average cross-section of forty-eight and one-half by fourteen and one-half feet, which gives, in the French system, a total air capacity of about two hundred and sixty thousand cubic meters. The provisions for ventilation are as follows:

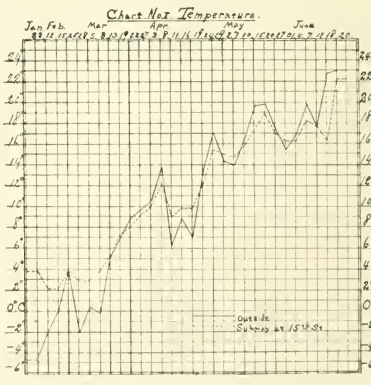
TABLE I.—Temperature.

Date.		Temperature. Outside.	Fifteenth St. Station.	Difference.	Weather.
1907					
Jan.	28	— 4.4°	3.8°	+ 8.2°	Clear.
Feb.	9	0.0	3.4	+ 3.4	Partly cloudy.
	11	1.9	3.1	+ 1.2	Clear.
	12	— 9.4	0.2	+ 9.6	Clear.
	13	— 2.5	0.0	+ 2.5	Clear.
	14	— 4.0	4.2	+ 0.2	Partly cloudy.
	15	— 1.8	2.5	+ 4.3	Clear.
	20	4.0	4.1	+ 0.1	Cloudy.
	21	2.0	3.5	+ 1.5	Clear.
	25	5.2	3.9	— 1.3	Clear.
	26	— 3.3	3.0	+ 6.3	Clear.
	27	0.8	3.3	+ 2.5	Clear.
	28	— 1.0	2.3	+ 6.3	Partly cloudy.
March	1	2.1	3.0	+ 0.9	Partly cloudy.
	4	— 3.1	2.2	+ 5.3	Partly cloudy.
	5	1.9	3.3	+ 1.4	Partly cloudy.
	6	0.5	3.6	+ 3.1	Partly cloudy. Snow.
	7	— 3.0	3.6	+ 6.6	Partly cloudy.
	8	2.2	4.2	+ 2.0	Partly cloudy. Snow.
	11	1.2	4.0	+ 2.8	Clear.
	12	4.1	4.2	0.2	Cloudy.
	13	8.3	6.0	— 2.3	Cloudy.
	14	9.2	6.9	— 2.3	Cloudy.
	18	9.0	9.7	+ 0.7	Clear.
	19	3.5	6.2	+ 2.7	Cloudy.
	20	6.0	6.6	+ 0.6	Clear.
	21	6.9	7.3	+ 0.4	Clear.
	22	13.6	10.3	— 3.3	Partly cloudy.
	25	7.0	8.5	+ 1.5	Clear.
	26	7.5	8.5	+ 1.0	Cloudy.
	27	13.9	10.7	3.2	Cloudy.
	28	16.0	13.0	— 3.0	Partly cloudy.
April	2	3.0	6.0	+ 3.0	Clear.
	3	13.0	11.0	2.0	Clear.
	4	14.4	12.1	— 2.3	Clear.
	5	19.5	14.1	— 5.4	Clear.
	8	7.5	10.2	+ 2.7	Cloudy.
	9	2.0	7.3	+ 5.1	Cloudy. Snowing.
	10	7.3	9.0	+ 1.7	Partly cloudy.
	11	9.0	10.5	+ 1.5	Partly cloudy.
	12	9.0	10.0	+ 1.0	Partly cloudy
	15	5.5	9.3	+ 3.8	Clear.
	16	11.6	10.5	— 1.1	Cloudy.
	17	8.5	10.0	+ 1.5	Partly cloudy.
	18	9.5	10.5	+ 1.0	Partly cloudy.
	19	2.2	8.2	+ 6.0	Cloudy. Snow.
	22	12.5	11.6	0.9	Clear.
	23	14.0	12.2	— 1.8	Partly cloudy.
	24	14.1	12.7	— 1.4	Clear.
	25	16.8	15.1	— 1.7	Clear.
	26	21.5	17.5	— 4.0	Clear.
	29	12.8	13.6	+ 0.8	Cloudy.
	30	16.3	16.0	0.3	Cloudy.
May	1	14.1	15.2	+ 0.8	Cloudy.
	2	12.6	13.6	+ 1.0	Cloudy.
	3	11.4	13.8	+ 2.1	Partly cloudy.
	6	15.1	15.3	0.2	Cloudy.
	7	15.6	15.3	— 0.3	Cloudy.
	8	17.7	16.0	— 1.7	Partly cloudy.
	9	12.8	14.2	+ 1.4	Cloudy. Rain.
	10	19.3	17.5	— 1.8	Clear.
	13	16.6	16.7	+ 0.1	Clear.
	14	22.6	18.3	— 4.3	Clear.
	15	20.5	17.0	— 3.5	Clear.
	16	25.5	21.0	— 4.5	Cloudy
	17	16.0	16.6	+ 0.6	Cloudy.
	20	17.8	19.1	+ 1.3	Cloudy.
	23	21.4	18.1	— 3.0	Cloudy.
	24	16.9	17.0	+ 0.1	Cloudy.
	27	13.6	16.2	+ 2.6	Cloudy.

TABLE I.—*Continued.*

Date.		Temperature Outside.	Fifteenth St. Station.	Difference.	Weather.
1907					
May	28	12.7°	15.4°	+ 2.7°	Clear.
	29	18.0	17.7	— 0.3	Clear.
	31	15.1	17.5	+ 2.4	Cloudy.
June	1	15.9	16.2	+ 0.3	Cloudy.
	3	16.6	15.5	— 1.1	Cloudy.
	4	18.6	17.7	— 0.9	Clear.
	5	19.0	18.2	— 0.8	Partly cloudy.
	6	21.6	19.4	— 2.2	Partly cloudy.
	7	19.0	17.6	— 1.4	Partly cloudy.
	10	21.0	18.6	— 2.4	Clear.
	11	15.8	17.4	+ 1.6	Cloudy.
	12	16.0	17.3	+ 1.3	Cloudy.
	14	14.5	16.0	+ 1.5	Cloudy.
	17	27.8	20.2	— 7.6	Partly cloudy.
	18	26.6	22.7	— 3.9	Partly cloudy.
	20	23.0	22.3	— 0.7	Partly cloudy.

Between Fifteenth Street and Eighteenth Street the north wall of the tunnel is pierced by four air-shafts, two of which are right in Fifteenth Street Station. These shafts rise to a distance of about five meters above the sidewalk against the wall of the Pennsylvania Railroad Trainshed. Inside they are open from floor to roof, the opening being equal to twelve and one-half square meters. Just east of the north



platform and just west of the south platform at Nineteenth Street Station are two larger ventilators, which open through an iron grating directly in the sidewalk. The area of these ventilators is eighteen square meters. At Twenty-second Street there is a ventilating stack which rises to a distance of eighteen meters above the street level, area of internal opening being five and one-fifth square meters. This stack was built at this point on account of the enormous leakage of

illuminating gas from the nearby reservoirs, which, in spite of a very effective current through the stack, causes a marked odor in the tunnel. In considering the ventilators we also took into account the air currents at the incline (west end of tunnel, where the cars come up to the surface or elevated), which, in the event of a northwest or west wind, were sometimes very strong.

Our observations were made in two sets. The first set gives conditions in cold weather (January and February) (see Table II). The second set covers the same ground in hot weather (May and June) (see Table III); except that during the early observations the two ventilators in Fifteenth Street Station were boarded up and, consequently, no mention of them is made in Table II. For convenience in tabulation the ventilators are numbered from 1 to 6, beginning at Fifteenth Street. An air meter of French make was used in all

TABLE II.—Ventilators.

Date.	Ventilator 3.	Ventilator 4.	Ventilator 5.	Ventilator 6.	Stack.	Incline.	Total inflow per minute.	Total outflow per minute.	Wind.
1907									
January 31	—	—	—	65 ↓	55 ↑	43 ↓	3965.0	286.0	N. E.
February 1	±	±	25.4 ↓	—	—	45 ↓	3382.2	—	N. W.
7	±	±	35.0 ↑	33 ↓	69 ↑	36 ↓	2934.0	989.0	W.
8	±	±	7.0 ↓	19 ↓	129 ↑	50 ↓	3718.0	670.8	N. W.
11	±	13 ↓	66.0 ↑	49 ↓	356 ↑	56 ↓	4685.0	3039.0	W.
12	—	18 ↓	63.0 ↑	26 ↓	179 ↑	54 ↓	4204.0	2065 0	N. W.
13	44 ↓	9 ↓	59.0 ↓	±	37 ↑	±	1730.0	192.4	S. W. S.
14	79 ↓	±	±	8 ↓	±	±	1139.0	—	S.
15	±	27 ↓	61.0 ↑	20 ↓	92 ↑	28 ↓	1520 0	5882.0	N. W.
20	±	±	65.0 ↓	98 ↓	56 ↑	44 ↓	5733.2	291.2	N. W.
21	±	28 ↓	±	±	284 ↑	97 ↓	6667.5	1476.8	N. W. W.
26	19 ↑	±	54.0 ↓	67 ↓	63 ↑	80 ↓	7337.6	567.0	N. W.
28	±	±	±	42 ↓	70 ↑	±	739.2	364.0	N. E.

TABLE III.—Ventilators.

Date.	Ventilator 1.	Ventilator 2.	Ventilator 3.	Ventilator 4.	Ventilator 5.	Ventilator 6.	Stack.	Incline.	Total inflow per min.	Total outflow per min.	Wind.
1907											
May 22	49 ↓	66 ↓	±	±	74 ↓	42 ↑	204 ↑	99 ↓	9198.0	1816.8	N. W., light.
23	±	±	±	±	±	±	19 ↓	18 ↑	98.8	1170.0	N. W., faint.
24	± ↓	± ↓	± ↓	±	±	± ↓	±	36 ↓	2310.0	0.0	S. W. S., light.
27	26 ↑	26 ↑	±	±	31 ↓	92 ↓	37 ↑	17 ↓	3319 0	847.6	N. W. N., light.
28	15 ↓	16 ↓	17 ↑	±	14 ↓	53 ↓	148 ↑	101 ↓	8161 6	983.8	W., fresh.
29	±	±	±	±	± ↑	36 ↓	± ↑	20 ↓	1948.0	0.0	N. W., light.
31	22 ↓	22 ↓	20 ↓	± ↓	26 ↓	22 ↓	31 ↓	20 ↓	3147.2	0.0	S. W., fresh
June 1	± ↑	± ↑	±	± ↓	26 ↓	54 ↓	35 ↓	± ↑	1622.0	0.0	E. N., light.
3	±	32 ↑	28 ↑	± ↑	31 ↑	68 ↓	67 ↑	49 ↓	4409.0	1716.4	N. W., light
4	19 ↓	22 ↓	29 ↓	25 ↑	21 ↓	26 ↑	24 ↓	25 ↓	3009 8	783.0	S. W., fresh
5	± ↓	19 ↓	19 ↓	± ↑	48 ↓	± ↓	88 ↑	23 ↓	2937 8	457 6	S. W., fresh
6	19 ↓	21 ↓	± ↑	± ↑	±	± ↓	110 ↑	47 ↓	3559.0	572 0	W. N., fresh + .
10	—	—	19 ↓	± ↓	11 ↑	76 ↓	37 ↑	± ↑	1697 4	930 4	N. E., light.
12	± ↑	± ↑	±	±	± ↓	34 ↓	31 ↑	± ↑	612 0	161 2	N. E., light

the observations, it having been carefully standardized in the beginning with an apparatus of similar design made in this country, and found to be very accurate. The tables are almost self-explanatory. The downward pointing arrow (↓) indicates a current flowing into the Subway, and vice versa. The figures are "meters per minute." The sign ± indicates a variable current without any decided tendency; ±↓ indicates a variable current, but with a tendency inward; ±↑ indicates a variable current with an outward tendency. (Of course, all of the currents vary temporarily with the passage of a car.) In the last three columns of the tables are given the total inflow and outflow in cubic meters per minute and the direction of the wind. A glance at these figures shows at once that they do not even approximately correspond. This discrepancy is readily explained by the fact that a large amount of air passes in and out through the stations, not to mention the sudden and frequent changes in the surface currents, which would, of course, affect the currents in the air-shafts. Several attempts were made to study the currents in the stairways and exits, but, owing to the constant passage of people to and fro the results were unsatisfactory. From the few observations made, however, we were able to demonstrate an outward movement as a car approached the station, and a tendency, though less marked, to produce an inward current as the car left the station. On one occasion (June 1st) at Nineteenth Street Station we noted a fairly definite outgoing current on the stairway, while both ventilators (see Table III) showed a decided incoming current at that time.

Taking a more careful survey of Table II, we find the currents through ventilators 3, 4, and 5 (ventilators 1 and 2 were boarded up) to be very variable, both as to strength and as to direction. Ventilator 6 showed an almost constant inward current, while through the stack the current was almost invariably outward. The relation, already mentioned above, between the direction of the wind and the current at the incline is now readily seen. The prevailing wind during February was northwest or west and the current at the incline was almost invariably inward, the exceptions being on days when the wind blew from another quarter. Of course, the influence of winds in the ventilators would be much less marked, unless the wind blew directly into the opening of the ventilator. Calculating the average inflow and outflow per hour from Table II, we find that the two hundred and sixty thousand cubic meters of air in the Subway could be renewed once in an hour, considering the tunnel as a whole. But this cannot be stated unreservedly, for we know that the longitudinal currents are not sufficiently marked to cause through and through ventilation, much of the air passing in at one ventilator and out the next, or in at the incline and out through the stack, thus ventilating only a small portion of the tunnel.

Table III hardly requires any special comment. Calculating the average per hour in the same way, we find the air in the tunnel could be renewed once in about an hour and fifteen minutes, so that the conditions are approximately the same in warm as in cold weather.

Estimating the total number of people in the Subway at the most crowded time of the day to be 3000 (maximum), there would, at the above rates of renewal, be a plentiful supply of fresh air.

It is, I believe, the intention of the Philadelphia Rapid Transit Company to place electric fans in the air-shafts. "At each end of each platform there is a ventilation chamber in which there will be installed an electric fan to exhaust the air from the Subway and discharge it into the street through a shaft."[7] The use of fans is pretty general in the English subways, and in New York and Boston they are used in the crowded sections. So far, there is no apparent need for them in the Market Street Subway, but in the section between Broad Street and the Delaware River, where surface rights are more expensive and air-shafts will, consequently, be fewer, the electric fan will, doubtless, be necessary.

We come next to a consideration of the influence of the movements of cars on air-currents in the Subway. Dr. Soper, working in the New York Subway, compared the phenomena observed to those of respiration.[8] The air forced out the ventilator by an approaching car and sucked in after the passage of the car is compared to tidal air. The similar but much greater effects caused by the express trains correspond with the supplemental air and complemental air in respiration; while the comparison of the residual air in each case is obvious While the above-described "out current as the car approaches and in current after its passage" may be said to be characteristic, it is by no means constant. We have noted outgoing currents, set up by an approaching car, which persisted thirty seconds after the car had passed. Again, if there is a strong current through a ventilator, independent of the motion of cars, it will vary only momentarily with the passage of a car. On the other hand, when there is little independent current, we have noted the approach of an express train twenty seconds before it passed, by the out current produced through the ventilator.

We were also much interested in studying the effect of the movements of the cars on the longitudinal air-currents in the tunnel. These observations were made at two points, which we will designate as point *X* and point *Y*, situated respectively at Seventeenth Street and at Twenty-first Street, and removed from the direct influence of any ventilator. The same air meter was used. It was placed midway between the tracks and at a height of about six feet from the roadbed. Following the passage of a local car there is a sudden, strong current in the same direction, of course, which lasts for ten or fifteen seconds and is followed by another strong current (really an exacerbation of the same current), persisting from

en to thirty seconds longer. The term "after-current" might be applied to this second current, while the term "following-current" would apply very well to the first. (Possibly some such terms are already in use.) When two cars follow each other at an interval of about fifteen seconds, the after-current of the first coincides with the following-current of the second, thus producing a current of greater strength and longer duration than usual. If the cars followed each other at intervals of not more than forty seconds, therefore, there would be produced a practically constant-current. We have noted this so-called after-current after the passage of express trains on surface railroads, and, taking into consideration the action of dust under these circumstances, are inclined to think that the effect is due to a spiral motion imparted to the air by the passage of the car and some slight inequality in the lateral resistance of the surrounding air, the tendency to produce a spiral motion under such conditions being a well-known physical fact. The apparent lull, therefore, is only that portion of the current during which the moving side of the spiral is at the top, the after-current being the second and longer turn of the spiral.

Besides the above-described current, there is always a counter-current set up in the opposite direction on all the other tracks, most marked, of course, on the nearest track. The counter-current is not so strong nor of so long a duration as the following- and after-currents and is frequently, almost invariably in the case of an express train, reversed entirely by the after-current. Between the outside wall and a local car the air meter indicates a slight advance-current ("piston action") as the car approaches, a strong current in the opposite direction during the passage of the car, and the usual following- and after-currents. The express trains cause similar currents to those produced by the local cars, but of correspondingly greater strength and longer duration.

We have already spoken of the current which enters at the incline when the wind is from the west or northwest. As a rule this current is dissipated when we get more than a hundred yards or so inside the tunnel; but on several occasions we were able, by exposing the air meter on each of the four tracks in succession, to demonstrate a decided eastward tendency at points X and Y. On at least one occasion (June 11th), with a fresh northeast by east wind, we noted a marked westward tendency at point X, with a less marked tendency in the same direction at Y. So that it is, at least, possible that, given a strong east or west wind, we might have, to a certain extent, through and through ventilation of the entire tunnel.

Next in order comes the subject of humidity. The so-called insensible perspiration in the human economy and the imperative necessity for its constant evaporation to the comfort and health of the individual render this subject of humidity of very great importance. This fact has long been recognized in both professional and popular literature. Rohé[9] speaks of the important relation between dry cold air and

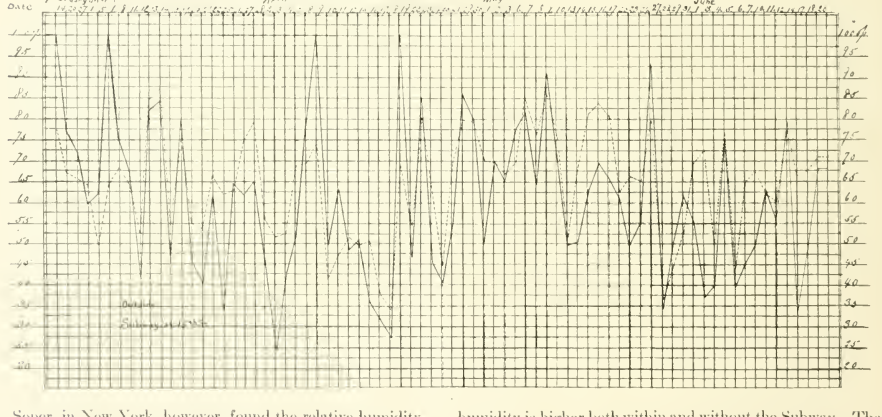
TABLE IV.—Humidity.

Date.		Outside.		Fifteenth St. Station.		Nineteenth St. Station.		Weather.
		Absolute.	Relative.	Absolute.	Relative.	Absolute.	Relative.	
1907			%		%		%	
Feb.	11	2.98	53.8	—	—	2.73	45.8	Clear.
	14	Raining.		4.97	77.0	4.53	74.5	Rain.
	20	4.89	76.7	4.31	67.2	3.62	60.7	Cloudy.
	27	3.69	71.7	4.02	66.1	3.43	63.1	Clear.
Mar.	1	3.31	59.0	3.82	64.0	3.67	65.8	Clear.
	5	3.44	62.2	3.02	49.6	3.25	56.4	Clear.
	6	Snowing.		3.92	63.1	3.44	62.2	Snow.
	8	4.14	75.0	4.35	67.4	3.91	65.8	Snow.
	11	3.24	61.3	4.07	63.8	3.40	60.6	Clear.
	12	2.40	36.6	3.33	51.6	3.82	62.8	Clear.
	13	6.89	81.9	6.04	83.1	5.88	88.8	Cloudy.
	14	7.47	83.8	6.68	86.9	6.79	95.4	Cloudy.
	18	4.09	46.5	4.86	52.8	4.89	64.8	Clear.
	19	4.91	79.7	5.80	78.9	—	—	Cloudy.
	20	3.29	45.3	4.15	55.0	3.72	52.9	Clear.
	21	3.11	40.4	4.23	53.6	—	—	Clear.
	22	7.16	61.0	6.40	67.0	—	—	Partly cloudy.
	25	2.64	34.1	5.29	62.0	—	—	Clear.
	26	5.17	64.7	5.41	63.4	—	—	Cloudy.
	27	7.34	61.4	7.33	74.7	—	—	Cloudy.
	28	8.81	65.0	8.81	78.1	—	—	Partly cloudy.
April	2	2.72	45.6	4.01	55.2	—	—	Clear.
	3	2.71	24.0	5.13	51.4	—	—	Clear.
	4	5.28	42.8	5.59	52.2	—	—	Clear.
	5	8.58	51.4	8.23	68.2	—	—	Clear.
	8	6.29	78.7	6.59	69.4	—	—	Cloudy.
	9	Snowing.		5.85	74.1	—	—	Snow.
	10	3.91	49.5	3.66	41.6	—	—	Partly cloudy.
	11	5.53	62.9	4.56	47.1	—	—	Partly cloudy.
	12	4.19	47.6	4.88	52.0	4.72	54.6	Partly cloudy.
	15	3.61	51.1	4.45	49.6	3.72	43.9	Clear.
	16	3.62	35.9	4.80	50.5	4.75	54.0	Cloudy.
	17	2.70	31.6	3.54	37.7	3.66	41.6	Partly cloudy.
	18	2.48	27.3	3.33	34.4	3.51	40.2	Partly cloudy.
	19	Snowing.		5.72	68.4	5.49	67.8	Snow.
	22	5.10	46.5	5.44	52.5	5.46	56.4	Clear.
	23	10.24	85.1	8.70	80.9	—	—	Partly cloudy.
	24	5.60	46.3	6.88	62.0	6.64	64.8	Clear.
	25	5.71	40.1	5.80	44.1	6.58	59.7	Clear.
	26	10.28	54.8	10.31	69.3	9.65	77.8	Clear.
	29	9.58	85.9	9.32	79.5	9.21	86.7	Cloudy.
	30	10.94	79.2	10.72	79.1	10.50	87.3	Cloudy.
May	1	6.25	50.7	9.06	70.1	—	—	Cloudy.
	2	7.68	69.6	8.17	69.7	7.70	72.5	Cloudy.
	3	6.61	61.8	7.91	66.6	7.36	66.4	Partly cloudy.
	6	9.92	77.2	9.00	69.2	9.13	77.3	Cloudy.
	7	10.85	82.0	11.04	84.9	10.44	87.3	Cloudy.
	8	9.34	62.0	10.31	76.1	—	—	Partly cloudy.
	9	10.10	90.5	10.50	86.2	10.10	88.3	Rain.
	10	11.40	69.1	11.28	75.9	11.18	86.0	Clear.
	13	6.99	49.7	7.31	51.6	—	—	Clear.
	14	10.31	51.5	10.62	68.1	10.44	77.1	Clear.
	15	11.07	62.6	11.75	81.6	11.92	80.7	Clear.
	16	16.31	69.3	15.16	83.2	13.95	90.6	Cloudy.
	17	8.94	66.0	11.31	80.4	10.48	80.6	Cloudy.
	20	9.14	60.3	10.24	62.4	—	—	Cloudy.
	23	9.04	48.5	10.41	66.5	—	—	Cloudy.
	24	7.96	55.6	9.38	65.1	8.81	65.7	Cloudy.
	27	10.89	92.9	10.87	79.2	—	—	Cloudy.
	28	3.81	34.3	4.76	36.3	4.11	33.5	Clear.
	29	7.51	48.9	6.66	44.2	6.87	52.5	Clear.
	31	7.96	61.9	8.36	56.2	8.09	61.5	Cloudy.
June	1	7.41	55.2	9.48	69.0	—	—	Cloudy.
	3	5.21	37.0	9.66	73.1	8.68	67.1	Cloudy.
	4	6.47	40.1	7.11	49.1	8.03	59.9	Clear.
	5	12.20	75.3	11.98	77.2	11.67	81.5	Partly cloudy.
	6	7.22	38.3	7.12	42.9	7.96	58.4	Partly cloudy.
	7	7.52	46.4	9.68	64.7	8.68	63.2	Partly cloudy.
	10	8.86	48.6	10.71	67.5	—	—	Clear.
	11	8.55	63.8	9.10	63.6	8.54	63.0	Cloudy
	12	7.50	55.3	8.90	60.6	7.96	57.2	Cloudy.
	14	9.91	79.9	10.72	79.1	9.94	74.6	Cloudy.
	17	8.96	33.4	11.57	66.6	10.40	63.0	Partly cloudy.
	18	12.39	49.5	13.50	67.1	13.15	77.0	Partly cloudy.
	20	13.86	67.7	14.06	74.5	13.69	80.6	Partly cloudy.

physiological conditions, especially of the respiratory tract. The extreme discomfort which follows a sudden rise in the relative humidity, especially when accompanied by a rise in temperature, is doubtless responsible, to a large extent, for the attacks of syncope which occur in crowded halls; and is doubtless, also, an important factor in such disasters as that of the Black Hole of Calcutta. It is a significant fact, too, that microörganisms thrive much better in the presence of moisture.

In the investigations conducted in the Boston Subway[6] the relative humidity was found to vary quite consistently with the temperature. Thus, for the warm months of September and October (1897,) May, June, July, and August (1898), we find the relative humidity almost invariably greater inside the tunnel. During the winter months, on the other hand, it was usually greater outside, the difference in temperature for the same time being in favor of the Subway.

February to June, including some 300 estimations of absolute and relative humidity. Our results correspond quite closely with those obtained in Boston. In cold weather (until March 11th) the relative humidity was generally greater outside. (See Table IV and Chart II.) From here until April 9th, when it snowed, it remained generally higher inside, covering a period of rather prematurely warm spring weather. From this point on the lines of the graphic chart frequently cross each other, following, with a fair degree of accuracy, the frequent and marked changes in temperature, until, on June 1st, it finally assumes what may be termed the normal summer relation, that is, a higher relative humidity inside the Subway than outside. It will be noted, also, that, while the average relative humidity outside fell from about 77 per cent. in February to about 50 per cent. in June, the average inside the Subway remained practically the same, about 64 per cent., for both periods. In cloudy weather, of course, the relative



Soper, in New York, however, found the relative humidity generally less in the tunnel throughout his investigations[10] (averaging 56.2 per cent. in the Subway). This may be explained by the relatively high temperature which pertains in the New York Subway, as has already been mentioned. The dew point, under these conditions, is actually higher in the Subway than in the street, but the much higher temperature in the Subway makes the relative humidity less. Smith[11] found the relative humidity in the Subway cars to vary from 53 to 66 per cent., according to the number of people in them.

In the Market Street Subway we used the ordinary wet- and dry-bulb thermometer, or psychrometer, at first as a "sling" psychrometer, but later finding it more convenient to use it in the usual way. The observations cover a period from

humidity is higher both within and without the Subway. The highest record was obtained at Nineteenth Street Station on March 14th, being on that occasion 95.4 per cent. Again, in the latter part of March, during some unusually warm weather, the relative humidity became so high that in parts of the tunnel there was visible precipitation of moisture on the cold steel columns. The results at Nineteenth Street show that the relative humidity there was greater on an average than at Fifteenth Street. On one or two occasions when the reading was made half-way between stations, it was found to correspond very closely with the readings made in the stations. Table V gives only the relative humidity, inside and outside the Subway, for morning and afternoon, showing a constant tendency to diminish in the afternoon.

TABLE V.—Humidity (Special).

Date.	Outside.		Inside.		Weather
	A. M.	P. M.	A. M.	P. M.	
1907					
April 21	46.3	27.7	62.0	13.3	Clear.
26	54.8	42.9	69.3	66.2	Clear.
29	85.9	61.1	79.5	78.4	Cloudy.
30	79.2	53.3	79.1	73.2	Cloudy.
May 2	69.6	61.6	69.7	64.7	Cloudy.
3	64.8	43.9			Partly cloudy.
8	62.0	49.6	76.1	73.2	Partly cloudy.
9	90.5	81.6	86.2	83.8	Rain.
10	69.1	40.4	75.9	53.6	Clear.
15	62.6	55.5	81.6	73.6	Clear.
17	66.0	58.1	80.4	73.7	Cloudy.
Average	68.2	52.1	75.9	68.3	

We come now to a consideration of that which makes the sky blue, which makes possible the thunder cloud and the mists of the morning, the omnipresent dust of the earth from which we are formed and to which we shall return. That the presence of particulate bodies of various sizes floating in the air has an influence, aside from any bacteriological consideration,* on the health of the individual breathing that air is a well-recognized fact. The mere mechanical irritation of large dust particles is, doubtless, sufficient to set up a simple inflammation of a delicate mucous membrane. This is readily illustrated by the "tickling sensation" complained of by subway employés, accompanied by the expectoration of dark, slate-colored mucus.

Of the literature on dust, Tyndall[12] has probably contributed most. (See under Bacteria.) Sir Oliver Lodge,[13] contrasting the pure air of Canada with the London fog, speaks of all foreign matter in the air as constantly sinking through the air toward the earth's surface, though borne upward from time to time by currents of air.

The sources of dust are manifold and need no enumeration. In a subway the chief sources are the wear and tear on running gear and the presence of human beings. In the New York Subway the following figures were obtained by a chemical analysis of the dust:[10] Metallic iron, 61.30 per cent.; organic matter, 21.94 per cent.; silica, etc., 15.58 per cent.; oil, 1.18 per cent. The excess of dust in the Subway over that in the street ranged from 11 to 800 per cent., averaging 47 per cent.

In the Market Street Subway we used the Aitken dust counter, making daily counts inside and outside the tunnel. This ingenious little instrument, probably known to everyone interested in hygiene, depends for its action on the fact that moisture will readily condense around an invisible dust particle and precipitate it as a visible globule of water. This precipitation is brought about in an air-tight, moisture-saturated chamber, into which a measured quantity of the dusty air has been admitted. The water globules are then counted by means of a small lens and a simple calculation gives the number of dust particles per cubic centimeter (Table VI). Mitchell Prudden[14] says of the Aitken dust counter: "It is

* For the sake of simplicity we will, as far as possible, consider the closely related subjects of dust and microorganisms independently.

TABLE VI.—Dust count.

Date.	Outside.	Fifteenth Street Station.	Nineteenth St. Station.	Temp.	Barometer	Weather.
1907						
Mar. 13	4000	4500	1000	8.3	755.0	Cloudy.
14	1500	4500	2000	9.2	854.0	Cloudy.
18	4000	2000	2400	9.0	768.0	Clear.
19	0	1500	—	3.5	760.5	Snow.
20	3000	4000	1500	6.0	757.0	Clear.
21	2000	2000	—	6.9	...	Clear.
22	4000	3500	—	13.6	754.9	Cloudy.
25	4000	1500	—	7.0	770.3	Clear.
26	3500	2500	—	7.5	763.8	Clear.
27	2500	4000	—	13.9	761.1	Clear.
28	3000	3000	—	16.0	759.9	Partly cloudy.
April 2	5500	3000	—	3.0	766.3	Clear.
3	5000	3500	—	13.0	766.6	Clear.
4	3500	2500	—	14.4	761.3	Clear.
5	2500	2500	—	19.4	752.9	Clear.
8	2000	1000	—	7.5	750.5	Cloudy.
9	0	1000	—	2.0	739.7	Snow.
10	3000	1500	—	9.0	743.5	Partly cloudy.
11	3000	1500	2000	9.0	753.5	Partly cloudy.
12	2000	2500	2500	9.0	753.4	Partly cloudy.
16	3000	2000	1500	11.6	754.2	Cloudy.
17	4000	2000	2000	8.5	755.7	Partly cloudy.
18	3000	3000	1000	9.5	760.1	Partly cloudy.
19	0	2000	1000	2.5	755.2	Snow.
22	3500	2000	2000	12.5	763.5	Clear.
23	1400	1200	—	14.0	752.6	Partly cloudy
24	1800	1600	1000	14.1	755.7	Clear.
25	3000	2000	1000	16.8	759.4	Clear.
26	6000	5000	4000	21.5	758.5	Clear.
29	2000	1800	2000	12.8	761.5	Cloudy.
30	2800	2600	1800	16.3	759.9	Cloudy.
May 1	3600	2800	—	14.4	763.8	Cloudy.
2	2800	2400	1800	12.6	766.7	Cloudy.
3	5000	4400	2000	11.4	765.0	Partly cloudy.
6	7000	3400	3400	15.1	761.7	Cloudy.
7	3000	3200	2800	15.6	756.8	Cloudy.
8	4400	3400	—	17.7	761.8	Partly cloudy.
9	0	1400	1600	12.8	751.1	Rain.
10	1400	1800	2000	19.3	756.4	Clear.
14	4800	2600	1200	22.6	759.7	Clear.
15	4000	2000	1200	20.5	760.4	Clear.
16	2600	2000	1200	25.5	756.9	Cloudy.
17	800	800	600	16.0	761.4	Cloudy.
20	400	800	—	17.8	757.8	Cloudy.
23	1600	800	—	21.4	762.4	Cloudy.
24	1200	1000	400	16.9	763.2	Cloudy.
27	0	1200	—	13.6	752.9	Cloudy.
28	3000	2000	600	12.7	759.9	Clear.
29	3200	1600	1400	18.0	758.7	Clear.
31	7600	2000	1600	15.1	762.8	Cloudy.
June 1	2000	1400	—	15.9	759.9	Cloudy.
3	1600	1200	400	16.6	750.4	Cloudy.
4	2600	2000	1600	18.6	760.9	Clear.
5	1400	2000	1800	19.0	752.3	Partly cloudy
6	4200	2400	1800	21.6	755.4	Partly cloudy
7	4200	1400	1600	19.0	759.5	Partly cloudy
10	3800	2600	—	21.0	762.6	Clear.
11	4200	2200	2200	15.8	761.0	Cloudy.
12	2000	1600	1800	16.0	764.2	Cloudy.
14	1000	800	600	14.5	755.6	Cloudy.
17	3000	2200	1200	27.8	766.9	Partly cloudy
18	2000	1200	1400	26.6	765.0	Partly cloudy
20	4000	1800	1400	23.0	760.2	Partly cloudy

the most accurate means of estimating the condition of the air in regard to dust." A glance at the table will show that the counts varied very widely, often without any apparent cause. There is, however, a distinct tendency for the count to be high in clear weather and low in cloudy weather; precipitation, of course, temporarily reducing the count to zero.

In the Subway we might expect less sudden and marked variations, but throughout our investigations there were men at work either right in Fifteenth Street Station or in the nearby excavations around City Hall. For example, on May 3d the workmen were tearing down some of the false work just east of Fifteenth Street. The count rose from 2400 the day before to 4400. Again, on April 24th, in the afternoon, shortly after the porter had swept the platform, the count was 2400. One-half hour later it fell to 1400. The same thing was noted outside. On May 6th the count went up to 7000 while the ash collectors were passing by. It is interesting to note that with a rapidly rising outside temperature—producing, therefore, a high relative humidity in the tunnel—the dust count is correspondingly diminished; thus, in the latter part of March, during that unusually warm period, we obtained on several occasions the same or even a lower reading in the Subway than out. The general tendency in cold weather, however, was for the count to be higher in the Subway. Thus, in April and May as the weather grew warmer we find the count higher in the street four times as often as in the Subway. In June this difference becomes even more marked. At Nineteenth Street Station the count is almost invariably lower than at Fifteenth Street, sometimes, therefore, being very much lower than outside. This is readily explained by the fact that the station is not completed on the north side and only a very few people make use of the east-bound platform.

TABLE VII. Dust count (special).

Date.	Outside.		Subway.		Weather.	
	A. M.	P. M.	A. M.	P. M.	A. M.	P. M.
1907						
April 24	1800	2400	1600	2400	Clear.	Same.
26	6000	6000	5000	6000	Clear.	Same.
29	2000	2800	1800	3400	Cloudy.	Clear.
30	2300	2800	2600	1600	Cloudy.	Same.
May 2	2800	4000	2400	3000	Cloudy.	Same.
3	5600	5200	4400	4000	Partly cloudy.	Clear.
8	4400	3200	3400	4000	Partly cloudy.	Same.
9	0	100	1400	800	Rain.	Cloudy.
10	4400	3400	1800	3600	Clear.	Same.
15	4000	6000	2000	2600	Clear.	Same.
17	800	1400	800	1400	Cloudy.	Partly cloudy.

Table VII shows the diurnal variation in the dust count. It will be noted that with one exception outside and three exceptions in the Subway the count rose in the afternoon. This is just as might have been expected, especially during the afternoon rush hours (4.30 P.M. to 6 P.M.) in the Subway.

Sir Oliver Lodge[13] has suggested the possibility of precipitating dust by means of a powerful electric discharge. This might be successful, but would be enormously expensive; and there is certainly no necessity for anything of the kind, under present conditions, in the Market Street Subway. We have purposely omitted any consideration of the relation between dust and microörganisms at this time, intending to take up that very interesting point under the head of microörganisms.

We have thus far confined ourselves to the first part of our title, namely, physical phenomena: temperature, ventilation, humidity, and dust. We come now to the consideration of a very important part of our work, which, while primarily chemical, will doubtless lead us into a discussion overlapping the biological end of the title. This interesting topic is air contamination due to the presence of human beings. The simple chemical interchange of oxygen and carbonic-acid gas in the lungs, with the consequent elimination of an excess of the latter gas in respiration, has long been regarded as an insufficient explanation of the phenomena which occur on breathing and rebreathing the same air. Knopf, speaking of the New York Subway,[15] remarks upon the foul odor after but two weeks' use. He goes on, in the same article, to speak of an "unknown substance of exceedingly unpleasant odor which emanates from human beings and which, in the absence of thorough ventilation, seems to settle on walls and floors." He believes it to be toxic in its nature, as it tends to produce nausea when first breathed after breathing fresh air. "It is present in tenement houses, almshouses, prisons, and in the New York Subway." This "unknown substance," under one name or another, has been the subject of much scientific speculation and research (perhaps more speculation than research). As early as 1802 we find a reference to this elusive substance. William Barnwell, surgeon in the employ of the Honorable East India Company,[16] after discussing the question from the standpoint of carbonic acid gas, says: " . . . we might as well expect to discover 'it' by mechanical as by any pneumatic instruments, . . . yet we are sensible of effluvia in the air which no instrument other than the olfactory nerve can discover." The presence of some such vague substance in sewer air made it for years a most dreaded substance. Thus, in 1879 and 1880, we find several important articles on the dangers of sewer air and its exclusion from houses.[17,18,14] Russia has contributed much to the literature on the chemistry and biology of air, the crowded, stuffy dwellings of the Russian pauper doubtless furnishing excellent material for this kind of research.

In 1880, Professor Ira Remsen gave an authoritative review of the subject up to that time.[20] After going over the methods for the estimation of organic matter in the air, he continues: " . . . . these organic constituents are the real mischief breeders, and, hence, the determination of the amount of organic matter in the air, provided it could be done

with accuracy, would give us a much more correct measure of its impurity than any means now employed. It is still customary to determine the amount of carbonic acid and from the quantity found to draw conclusions concerning the impurity of the air; but as the carbonic acid is known not to be the really injurious constituent, the method is obviously objectionable. We may have a very impure air without carbonic acid and a harmless air with a considerable quantity of that gas." Pettenkofer arrived at, practically, the same conclusions. Remsen's method was to aspirate the air through freshly ignited pumice stone, which was subsequently subjected to distillation and the free and albuminoid ammonia then estimated. Rebreathed air gave more than the usual amount of albuminoid ammonia. The breath of one individual for twenty-four hours yielded two-tenths of a gram of organic matter. Hermans, in 1883, endeavored to find organic matter in condensed expired air, but failed entirely. Carnelly[21] found the carbonic acid to vary with the amount of organic matter, but the variations of the organic matter were far wider and more rapid than those of the carbonic acid. One year later J. S. Haldane makes the following statement, which is somewhat at variance with a still later statement by the same authority (*vide infra*):[22] "It is a mere assumption and, as we shall see, an unjustified assumption, that the carbonic acid is anything like a certain measure of the impurities which are, directly or indirectly, communicated by human beings to the air in other ways than by respiration."

In 1888, Brown-Séquard and d'Arsonval astonished the scientific world by announcing the discovery of a "volatile alkaloid" (leukomain) which they had demonstrated in expired air.[23] They obtained a solution of expired air by pouring distilled water into the bronchial tubes of animals, and also by the condensation of breath. This solution they injected into rabbits and dogs, producing, practically, the symptoms of shock, and even death in some cases. After death the venous blood was red. Later in the same year a series of experiments was made on rabbits. These rabbits were so arranged that they all breathed the same air in succession, the last one receiving air which had been breathed by all the others. The results of these experiments served to confirm their belief in the new alkaloid. Moreover, they found that on passing the rebreathed air through sulphuric acid it lost its toxic properties, thus demonstrating a probable connection between the alkaloid and carbonic acid. Dastre and Loye,[24] in the same year, produced similar effects with large quantities of the fluid; also (dies infaustus) with large quantities of sterile water. Merkel,[25] on the strength of the rabbit experiments, concluded that the alkaloid must exist. Lehmann and Jensen,[21] also Hoffmann-Wellenhof,[27] late in the same year, found no trace of the alkaloid. Rauer[28] failed to verify any of the Brown-Séquard and d'Arsonval experiments. In 1892, Haldane,[29] after experimenting on human beings in an air-tight chamber, concluded that the "immediate" danger is from increased carbonic acid and diminished oxygen, and is not due to a specific poison. Bergey,[30] three years later, after carefully repeating the Brown-Séquard experiments, arrived at, practically, the same conclusion, finding "no peculiar poisonous organic matter in expired air." In July of the same year (1895), Dr. Hannah B. Clark, of Chicago University, published an excellent review of the literature upon this subject, from which we have extensively quoted.[24] Dr. Clark thinks that while carbonic acid is not dangerous *per se*, it is a good index of the impurity due to organic matter. Coming still nearer to the present day, we find some interesting matter on ocholitic poisoning in the *Sanitary Record* for August 20, 1897. Edward T. Willoughby in this article concludes that there is some organic matter of ill-understood and indefinite character in expired air, and still more in the exhalations of the body, with which, of course, the air of a crowded room becomes charged. He dwells particularly upon the exhalations of unclean bodies as the chief factor, comparing very appropriately, the odor of a crowded ballroom with that of a police court. Speaking of the poisonous properties of the exhalations from the body, it is interesting to note that Seleni has isolated from the skin of cadavera certain "cadaveric ptomains" which are more deadly than the purest aconitine.* John Hartley, F.R.C.S. Eng.,[31] believes that expired air contains a poison somewhat similar in its effects to the action of muscarine, as described by Lauder Brunton. Thus, we find eminent authorities on both sides of this question, and there is no middle course for the politic to pursue. Personally, we are inclined to think that the volatile alkaloid of Brown-Séquard and d'Arsonval does not exist. Bergey[30] says: "The two great causes of discomfort in an overcrowded, ill-ventilated room are excessive temperature and unpleasant odors." To these we would add a third. The sudden increase in the relative humidity in a crowded room, due to the evaporation of perspiration and the accumulation of moisture-saturated expired air, is doubtless one of the chief factors in the production of the so-called toxic symptoms.

Whatever may be the final word in this interesting discussion, it is certain that, at the present time, the only reliable index of air contamination by the presence of human beings is the estimation of the amount of carbonic acid in the air. The composition of ordinary fresh air is approximately as follows: Nitrogen, 78.49 per cent.; oxygen, 20.63 per cent.; water, 0.84 per cent.; carbonic acid, 0.04 per cent.[32] Dr. Keller,[33] of this city, estimates the carbonic acid at 0.03 per cent., or 3 parts in 10,000. Uffelman gives 3 or 4 parts in 10,000 as normal. In 1882, de Saussure, working with an apparatus to be described later, obtained the following very high figures: 0.0479 per cent. in winter and 0.0718

* Cadaveric ptomains are believed to have been known, in a crude form, to the Medician poisoners.

per cent. in summer. He subsequently got much lower results. Thenard, using a similar apparatus, gave 0.0391 per cent. as an average. The normal amount of carbonic acid, then, may be said to vary from 0.03 per cent to 0.04 or even 0.05 per cent. What, then, constitutes the upward limit of safety? Hermans, in 1883, placed the danger point at 3 per cent. Haldane and Smith,[32] in their experiments on human beings, noted hyperpnea at 3 to 4 per cent. At 10 per cent. extreme distress was produced. These figures, of course, indicate the extreme limit: 0.1 per cent. is usually regarded as the limit of safety; while E. E. Smith, of New York, has recently given 0.07 per cent. as the upper limit.[33]

Practically all of the methods for the estimation of the amount of carbonic acid are based upon its absorption by an alkaline solution. One of the earliest and simplest devices is the so-called Wolpert's air tester.[34] This is a simple transparency test with lime-water, rendered more or less opaque by the absorption of carbonic acid from the air passed through it. In 1882, two French scientists, A. Müntz and E. Aubin, published a series of results with the apparatus of de Saussure, already mentioned.[34] This consisted of a rubber balloon of fourteen liters' capacity into which was placed a known quantity of baryta-water. The titer of the baryta-water before and after its precipitation by the carbonic acid as an inert carbonate was ascertained, and from these figures the amount of carbonic acid was determined. With this apparatus fairly accurate results were obtained, an increase in the proportion of carbonic acid being noted in cloudy weather, with a further increase during a storm. Brunner obtained very similar results by passing large measured quantities of air through a tube containing moistened limestone, the rest of the process being similar to the above. The same principle is employed in the classic flask method of Pettenkofer, which is too well-known to require any explanation here. The Pettenkofer method, however, requires the use of bulky, cumbersome apparatus, and for a long time some simple, accurate method has been sought. In 1901, Haldane, an English scientist, whom we have already quoted several times, described an extremely ingenious apparatus for this purpose.[37] We obtained one of these little machines from a London firm and used it in our work in the Subway; and, while it had certain peculiarities, it improved with use and was on the whole very satisfactory. The apparatus accurately measures the volume of a specimen of air before and after the absorption of the carbonic acid by a solution of potassium hydroxide. The difference in volume is indicated on a scale which is so constructed as to read directly in parts of carbonic acid per 10,000 of air. It is extremely sensitive (we have seen the reading vary perceptibly when the draft from a passing car blew on the apparatus), making it necessary to always take an average of two or more readings. In very cold weather the solutions froze so that we were unable to begin our observations regularly until the middle of March. Moreover, there is a distinct tendency to get a higher reading in warm weather than in cold. We think we have seen this same tendency with the Pettenkofer method also. In a series of parallel observations, made at the suggestion of Dr. Abbott, with the Haldane apparatus and the Pettenkofer method, we obtained the following figures for laboratory air: Pettenkofer method, average, 5.9 parts per 10,000; Haldane apparatus, average, 5.7 parts per 10,000.

Two years ago another Englishman, Horace T. Brown, described an apparatus for the estimation of carbonic acid in the air which, while it gave excellent results in the hands of the originator, has not, so far as we know, ever been put to any practical use.[38] It depends for its action on the fact that air, containing a constant proportion of carbonic acid, will, if caused to pass in a turbulent stream over the free surface of a caustic alkaline solution, be absorbed with increasing rapidity up to a certain optimal speed. At this optimal speed, if the temperature remains constant, the rate of absorption will vary with the partial pressure of the carbonic acid, from which variation the amount of carbonic acid is estimated by a more or less complicated calculation.

The possibility of regenerating the atmosphere of buildings, tunnels, subways, etc., is a subject worthy of brief consideration. In 1882, Dr. Neale, of London, designed his so-called "chemical lung"[39] for the purification of the air in the Underground Railway. This apparatus consisted of two large rollers over which ran a continuous sheet of loosely woven cloth. The upper roller was moved by clockwork, the lower being immersed in a strong solution of potassium hydroxide, thus keeping the cloth constantly saturated. This, it was claimed, would not only absorb carbonic acid but also organic matter from the air. Whether the "chemical lung" ever got a chance to breathe in the London Subway or not we are unable to say. Other devices, depending on the fact that sodium dioxide and carbonic acid react with the formation of free oxygen, have been suggested; and recently the possibility of electrically dissociating the carbonic acid has been advanced. While it is possible to produce these results in laboratory experiments it is certainly safer, at the present state of our knowledge, to depend on a constant supply of fresh air by means of ventilation.

Glancing for a moment at Table VIII, we find that the amount of carbonic acid, even in street air, is by no means a fixed quantity. The close proximity of the Pennsylvania Railroad Depot to the Fifteenth Street Station, and especially to the point where the comparative outside observations were made, must be remembered in considering this table. Thus, on several occasions the amount of carbonic acid was actually higher at Fifteenth Street outside the Subway than at Nineteenth Street inside, due, no doubt, to the smoke from the engines in Broad Street Station. The fact, already mentioned,

that Nineteenth Street Station was very little used and the presence of a large ventilator at either end of the station explain why the air at this point was so much better than at Fifteenth Street Station. The outside readings averaged 4.8 parts per 10,000, being slightly higher (5.1) in cloudy weather. This agrees in the direction of variation with the work of Müntz and Aubin.[34] At Fifteenth Street Station the readings averaged 6.5, the highest record being on March 19th, a cloudy, snowy day, when the carbonic acid rose to 8.6 parts per 10,000. The lowest reading was 4 on May 17th. These results are somewhat higher than those obtained by Dr. Soper in the New York Subway.[8] Using the Pettenkofer flask method he found 4.58 parts per 10,000 in the Subway and 3.45 in the street, the highest single record in the Subway being 8.89. Smith,[11] working on the air inside the cars, found the carbonic acid to vary from 5.9 to 8.5, depending on how nearly crowded the car happened to be. Butterfield[37] found the air in the House of Commons to contain from 3.39 to 5.39 parts of carbonic acid per 10,000.

TABLE VIII.—Carbonic acid.

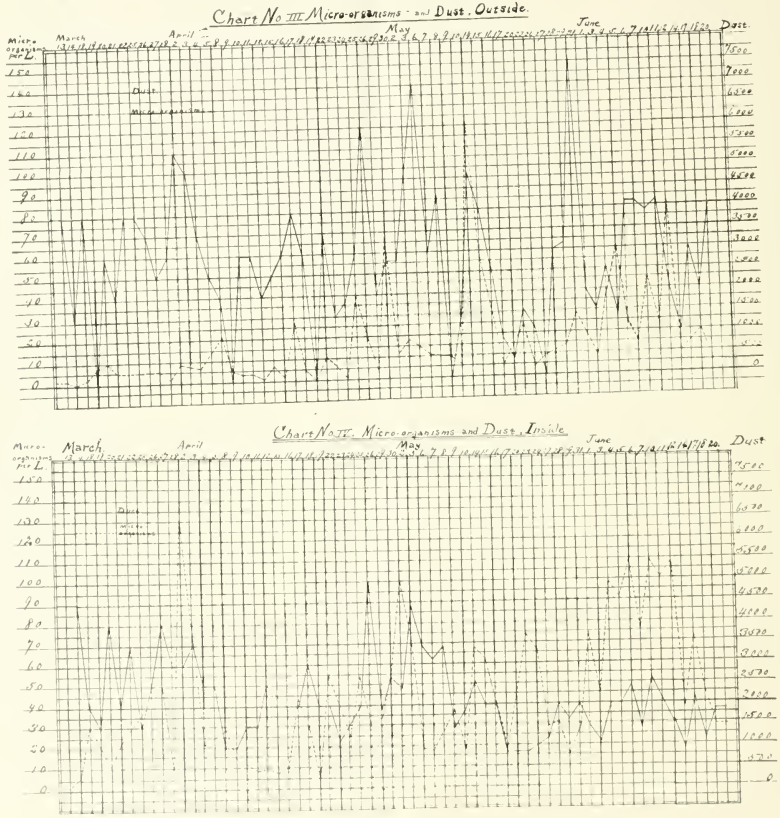
Date.	Outside.	Fifteenth Street Station.	Nineteenth St. Station.	Temp.	Barometer	Weather.
1907						
Mar. 15	5.7	8.0	—	..	..	Clear.
16	4.6	7.1	—	..	..	Clear.
18	5.0	6.5	4.5	9.0	768.0	Clear.
19	4.2	8.6	—	3.5	760.5	Cloudy, snow.
21	4.4	7.1	—	6.9	..	Clear.
22	4.0	6.0	—	13.6	754.9	Cloudy.
25	4.9	6.5	—	7.0	770.3	Clear.
27	4.0	5.5	—	13.9	761.1	Clear.
28	3.5	7.0	—	16.0	759.9	Partly cloudy.
April 2	4.2	5.0	—	3.0	766.3	Clear.
3	4.7	5.7	—	13.0	766.6	Clear.
4	4.2	5.5	—	14.4	761.3	Clear.
5	4.5	6.2	—	19.4	752.9	Clear.
8	6.0	6.7	—	7.5	750.5	Cloudy.
9	5.0	7.0	—	2.0	739.7	Cloudy, snow.
10	4.2	6.7	—	9.0	743.5	Partly cloudy.
11	4.5	7.0	5.8	9.0	753.5	Partly cloudy.
12	6.0	8.0	5.0	9.0	753.4	Partly cloudy.
15	4.5	7.0	5.2	5.5	..	Clear.
16	4.9	7.0	4.9	11.6	754.2	Cloudy.
17	4.4	6.0	4.5	8.5	755.7	Partly cloudy.
18	4.0	5.9	5.2	9.5	760.1	Partly cloudy.
19	5.2	6.9	6.2	2.2	755.2	Cloudy, snow.
22	3.5	5.3	4.9	12.5	763.5	Clear.
23	4.0	6.4	—	14.0	752.6	Partly cloudy.
24	3.7	5.7	—	14.1	755.7	Clear.
25	3.8	5.0	4.2	16.8	759.4	Clear.
26	3.3	5.3	4.3	21.5	758.5	Clear.
29	5.5	5.6	4.3	12.8	764.5	Cloudy.
30	4.7	5.8	4.7	16.3	759.9	Cloudy.
May 1	5.5	8.0	—	14.4	763.8	Cloudy.
2	6.4	7.0	5.4	12.6	766.7	Cloudy.
3	4.5	6.7	4.3	11.4	765.0	Partly cloudy.
6	4.7	6.0	5.4	15.1	761.7	Cloudy.
7	5.0	6.0	5.5	15.6	756.8	Cloudy.
8	5.2	5.5	—	17.7	761.8	Partly cloudy.
9	5.3	7.0	5.5	12.8	754.1	Rain.
10	3.7	6.2	4.8	19.3	756.4	Clear.
13	3.6	4.6	—	16.6	765.5	Clear.
14	3.5	7.0	3.9	22.6	759.7	Clear.
15	3.0	5.2	4.9	20.5	760.4	Clear.
16	5.0	5.0	5.0	25.5	756.9	Cloudy.
17	5.0	4.0	4.0	16.0	761.4	Cloudy.
20	4.0	4.0	—	17.8	757.8	Cloudy.
23	6.0	6.0	—	21.4	762.4	Cloudy.
24	6.0	7.5	5.0	16.9	763.2	Cloudy.
28	6.0	7.0	7.0	12.7	759.9	Clear.
29	5.0	6.2	5.5	18.0	758.7	Clear.
31	6.5	6.5	—	15.1	762.8	Cloudy.
June 1	6.5	6.7	—	15.9	759.9	Cloudy.
3	6.5	6.5	6.0	16.6	750.4	Cloudy.
5	6.0	7.0	6.0	19.0	752.3	Partly cloudy.
6	5.0	6.0	5.0	21.6	755.4	Partly cloudy.
7	4.4	5.7	—	19.0	759.5	Partly cloudy.
10	4.0	8.0	—	21.0	762.6	Clear.
11	5.0	7.0	6.2	15.8	761.0	Cloudy.
12	6.2	6.7	5.2	16.0	764.2	Cloudy.
14	6.5	6.5	6.0	14.5	755.6	Cloudy.
20	6.0	7.5	—	23.0	769.2	Partly cloudy.

We attempted to make some readings in the tunnel itself, away from stations or ventilators, but the difficulty and danger of manipulating the apparatus in the narrow space between the tracks limited our efforts in this direction considerably. The results obtained would average about the same as those obtained in the stations. In the pump-room at Twenty-second Street on May 27th we obtained a reading of 11, due, of course, to the proximity of the gas reservoirs.

Accepting 0.1 per cent. or 10 per 10,000 as a fair limit of safety (in London 13 per 10,000 is so-called "normal allowance"),[4] the air in the Market Street Subway may, as far as carbonic acid is concerned, be regarded as perfectly safe.

We will now take up the consideration of the last phase of our subject, the biological condition of the Subway air. The presence of minute living organisms in the air early excited the curiosity of scientific investigators. The long and bitter controversy over the theory of spontaneous generation turned upon this point. Such names as Needham, Spallanzani, and Treviranus in the beginning, and later Hoffman, Chevreul, Pasteur, and Tyndall, illumine the pages of this discussion. We are interested particularly in the methods employed. From the tiny drop of rain-water in which Leeuwenhoek (1675) detected living "animalcules" was gradually evolved the liquid media. With these vegetable and animal infusions Tyndall[42] did his classic work on floating matter in the air, and Pasteur, contending on the same side of the spontaneous generation theory, found the air of the Mer de Glace devoid of generative power, also the air of the caves under the Paris Observatory. A pure culture with this method was almost impossible and anything like a numerical result was out of the question. Then came the solid medium, gelatin, suggested by Koch, and adapted by Hesse (1884) to air examination. A glass tube was lined with a film of sterile gelatin and a measured quantity of air slowly aspirated through the tube. The microörganisms, falling on the surface of the gelatin, develop and are then readily counted. The exposure of a film of sterile gelatin in a Petri dish also early suggested itself as a means of ascertaining the number of organisms falling in a given time on a certain area. Percy Frankland[40 41] improved upon all previous methods by filtering the air through plugs of sterilized glass-wool, which, however, were

not plated but shaken up in a flask of melted sterile gelatin which solidified as a film on the inside of the flask. The use of the plate method was a natural outgrowth of the above. Various substitutes for the glass-wool plugs have been suggested. Dr. Greenleaf Tucker, of Boston,[42] used granulated sugar in a very narrow tube. Petri used calcined sand. Butterfield[37] in the House of Commons used glass-wool, placing a third plug, which he discarded in making the plates, in the proximal end of the tube. In our investigations we used the glass-wool plug, using a fine grade of glass-wool and packing it tightly. Only two plugs were used, the frequency with which the second remained sterile being sufficient justification for not using a third. Dry heat was used for sterilization because steam made the plugs stick in the tubes. One liter of air was aspirated through the plugs, which were then plated in agar at 40° C. and incubated at room temperature for six days.



Returning for the moment to the classic work of Tyndall on the floating matter in the air, we wish to discuss the relation between dust and microörganisms, already suggested under the head of dust. That such a relation exists is, we think, a generally accepted fact. It remains to be seen whether or not anything like a mathematical relationship can be demonstrated. That dustless air is sterile has been abun-

dantly proven. Tyndall[42] found optically pure air (air from which all the dust had settled so that a ray of light passing through it was invisible from the lateral aspect) incapable of setting up fermentation in vegetable and animal infusions. Pasteur, already quoted, found the dustless air of the Mer de Glace and of the caves under the Paris Observatory sterile. In the Bernese Alps de Freudenreich[43] found only eight bacteria in 2325 liters of air at elevations ranging from 2000 to 4000 meters. Christiani[44] in a balloon obtained sterile cultures at elevations of 1000 meters or more, and thought that, "Even at much lower levels the majority of the colonies came from the earth indirectly, *i. e.*, by way of the balloon." Leven[45] found only three bacteria and a few molds in 21,600 liters of air in the Arctic regions. More than a few miles out at sea the air has been found to be sterile. In all of these places dust is an unknown quantity. Tyndall did not contend that the microörganisms were always carried as passengers on the floating matter (dust) in the air. In fact, he definitely states that the "germs of bacteria" are capable of floating free in the air; but any process (in Tyndall's experiments simply settling by gravitation) which removes the dust from the air removes at the same time the microörganisms. This is demonstrated in Lister's classic explanation of the absence of infection in a traumatic emphysema. St. Clair Thompson and R. H. Hewlett[46] found normal expired air to be sterile for the same reason.

In the hope of demonstrating some coincidence in the rise and fall of the dust and bacterial counts we have made graphic charts of these observations, inside and outside of the Subway. (See Charts III and IV.) Of course, both of these counts are subject to such sudden and wide variations that, only by the accumulation of an enormous amount of data could anything positive be stated in regard to their relation. But the fact remains that, in places at least, these charts show a decided tendency to vary simultaneously and in the same direction. At the suggestion of Dr. Bergey we exposed, on several occasions, in various parts of the Subway and outside, Petri dishes containing a film of sterile agar. As soon as a colony became visible to the naked eye (usually in about twenty-four hours) it was carefully examined microscopically for the presence of foreign matter—dust. Invariably our search was rewarded, sometimes in the form of comparatively large, irregular masses looking like coal, and sometimes in the form of a tiny speck. It is interesting just to mention, at this point, Sir William Thomson's theory that the original "life germs" were brought to this planet on meteoric dust.

Glancing now at Table IX, we find a record of the number of bacteria and molds inside and outside of the subway from the middle of February to the latter part of June, including, therefore, winter, spring, and summer weather. For the sake of simplicity only the molds were counted separately, the saccharomyces and actinomyces, of which large numbers were

TABLE IX.—Bacteriological.

Date.		Fifteenth Street.				Nineteenth Street.				Weather.
		Outside.		Inside.		Outside.		Inside.		
		Bacteria.	Molds.	Bacteria.	Molds.	Bacteria.	Molds.	Bacteria.	Molds.	
1907										
Feb.	14	2	1	2	0	3	3	1	4	Partly cloudy.
	15	0	0	5	2	5	2	7	5	Clear.
	20	0	0	11	8	0	0	0	1	Cloudy, slush.
	21	4	6	6	0	0	1	0	0	Clear, slush.
	26	0	0	44	19	0	0	3	1	Clear, slush.
	27	0	0	4	0	0	1	2	0	Clear, slush.
March	1	1	0	4	8	—	—	7	1	Clear, slush.
	5	2	1	3	0	—	—	3	1	Clear, slush.
	6	6	1	7	14	1	0	4	2	Snowing.
	7	4	1	44	14	—	—	4	4	Clear, freezing.
	8	4	2	7	22	2	2	2	3	Snowing.
	11	0	0	1	2	1	0	3	0	Clear, slush.
	12	0	0	8	1	1	2	6	6	Clear, slush.
	13	1	0	0	1	4	1	0	1	Cloudy, slush.
	14	0	0	6	0	0	0	9	2	Cloudy, slush.
	18	2	0	8	23	14	0	16	4	Clear, slush.
	20	8	2	12	0	23	4	17	1	Clear, windy.
	21	3	1	14	9	—	—	—	—	Clear.
	27	6	0	42	8	—	—	—	—	Cloudy.
	28	1	0	7	1	—	—	—	—	Partly cloudy.
April	2	8	0	51	80	—	—	—	—	Clear.
	4	7	0	19	2	—	—	—	—	Clear.
	8	17	5	20	7	—	—	—	—	Cloudy.
	9	5	0	8	6	—	—	—	—	Cloudy, snow.
	10	4	0	12	0	—	—	—	—	Partly cloudy.
	11	3	0	8	0	—	—	—	—	Partly cloudy.
	12	1	0	9	0	—	—	—	—	Partly cloudy.
	15	5	2	6	0	—	—	—	—	Clear.
	16	2	0	11	0	—	—	—	—	Cloudy.
	17	28	0	44	0	77	1	0	16	Partly cloudy.
	18	5	0	28	0	11	0	23	1	Partly cloudy.
	19	1	0	5	0	2	0	3	1	Cloudy, snow.
	22	11	0	55	0	37	1	37	1	Clear.
	24	1	0	23	2	59	78	41	0	Clear.
	25	39	1	51	3	32	8	37	4	Clear.
	26	16	4	27	4	28	1	60	10	Clear.
	29	0	3	27	6	35	5	11	4	Cloudy.
	30	51	18	32	24	33	1	13	3	Cloudy.
May	2	10	2	60	41	33	3	98	13	Cloudy.
	3	17	0	63	10	51	3	38	2	Partly cloudy.
	6	9	5	17	1	24	2	128	3	Cloudy.
	7	6	5	6	11	17	8	8	13	Cloudy.
	9	7	3	16	21	16	5	6	0	Cloudy, rain.
	10	6	0	15	2	12	1	7	1	Clear.
	14	121	0	55	12	19	3	22	0	Clear.
	15	55	2	59	4	202	3	*	2	Clear.
	17	5	0	13	4	12	0	9	1	Cloudy.
	23	23	3	71	3	—	—	—	—	Cloudy.
	24	4	0	32	34	39	4	39	5	Cloudy.
	27	9	0	11	17	—	—	—	—	Cloudy.
	28	11	1	31	1	57	4	—	—	Clear.
	29	12	2	13	1	68	6	86	3	Clear.
	31	29	1	26	3	25	1	67	3	Cloudy.
June	1	17	2	58	16	—	—	—	—	Cloudy.
	3	7	1	37	8	50	8	32	8	Cloudy.
	4	17	10	86	12	64	38	64	19	Clear.
	5	31	21	54	11	21	33	37	37	Partly cloudy.
	6	23	1	83	25	61	90	64	6	Partly cloudy.
	7	12	3	63	13	59	7	49	13	Partly cloudy.
	10	39	13	52	56	—	—	—	—	Clear.
	11	22	2	63	18	98	11	74	10	Cloudy.
	12	68	15	59	48	128	4	84	20	Cloudy.
	14	9	0	30	8	22	4	25	3	Cloudy.
	17	14	0	58	15	116	15	132	12	Partly cloudy.
	18	19	2	42	3	41	1	55	6	Partly cloudy.
	20	4	1	26	3	18	1	25	7	Partly cloudy.
Average		13	0 2	1	28 3	10	5	31 1	7	8 28 2 5 3

* Countless.

found, being counted as bacteria. It will be seen that the average number of microörganisms is greater in the Subway than outside, the relation being approximately as 1 to 1.27. This is in marked contrast to the results in New York where Soper found a little more than twice as many in the street as in the Subway. Moreover, the actual numbers found in New York were only about 0.1 as great as ours. This last fact is probably due to difference in technique. In New York the plates were incubated at 37° C., which is not the optimum temperature for most of the air organisms; the colonies were counted at the end of forty-eight hours; we waited six days; and sand was used instead of glass-wool as the filtering material. At Nineteenth Street our results correspond more nearly to those obtained in New York. This difference between Fifteenth Street and Nineteenth Street Stations is explained by the unused condition of the latter; while the variation in the outside results is explained by the points of observation. At Nineteenth Street we were compelled to obtain our samples right at the head of the station stairway, in an exposed position, and near the level of the sidewalk. At Fifteenth Street, on the other hand, we were able to use our apparatus at a more convenient distance from the sidewalk, and in a position much less exposed to the dust of traffic. It will be seen from the averages at the end of the table that there was a disproportionately large number of molds in the subway. This agrees with the results in New York,[35] where E. E. Smith explained it by the absence of light, presence of moisture, and of currents of air which distribute the spores from place to place. A few observations were made at point *X*. The number of bacteria was low, molds being proportionately high.

Of course, there was an increase both inside and outside the Subway as the warm weather approached, the proportion of increase being very much greater outside than inside, as shown by the following figures: Average number of microörganisms at beginning outside, equal 2.6; average number of microörganisms at beginning inside, equal 12.2; average number of microörganisms at end outside, equal 57.0; average number of microörganisms at end inside, equal 75.1.

A short series of morning and evening observations has been tabulated (see Table X), showing a slight tendency to increase in the afternoon both outside and inside the Subway.

No studies were made of dust other than those already mentioned. In New York the dust from hand-rails, doors, etc., was found to be relatively free from bacteria.[15]

As to the sources of bacteria in a subway, Soper[15] thinks that most of them come from the street, adding, however, that "there is excellent ground for concluding that some, and among them the most objectionable kinds, are due to the presence of people." He did not, however, identify any of the organisms found. In our work it was, of course, impossible to follow out every colony. We attempted to select from day to day the unfamiliar organisms for cultivation. These were grown on the usual media and identified, as far as possible, with known species. Even by this method very many organisms must inevitably have been overlooked. The magnitude of an exhaustive study of this kind is too readily appreciated, however, by those familiar with bacteriological technique to require any further explanation. The following is a list of the organisms identified, given in alphabetical order:

Micrococcus æthebius.
Micrococcus candicans.
Micrococcus cremoides.
Micrococcus flavus.
Micrococcus orbicularis (Ravenel).
Micrococcus roseus.
Micrococcus simplex (Wright).
Sarcina alba.
Sarcina aurantica.
Sarcina flava.
Sarcina lutea.
Pseudomonas fluorescens.
Bacillus mesentericus.
Bacterium finitimum.
Bacterium helvolum.
Bacterium mycoides.
Bacterium palidor.
Bacterium subochraceum (Dyar).

There was also a pale-pink sarcina which occurred quite frequently. We could not find this organism in any of the text-books, and, as far as we know, Dr. S. J. Deehan, of the Laboratory of Hygiene, University of Pennsylvania, was the first to describe it.

Table X.—Bacteriological (special).

Date.	Outside.		Inside.	
	A. M.	P. M.	A. M.	P. M.
1907				
April 24	1	18	25	36
26	20	9	31	43
29	3	35	33	38
30	69	14	56	16
May 2	12	16	101	132
3	17	174	73	71
8	13	24	36	76
9	10	5	37	6
10	6	25	17	53
14	121	21	67	81
15	57	8	63	16
17	5	9	17	16
Average	27.8	29.8	46.3	48.6

In regard to the effect on the health of Subway employés, of their life underground, no routine method of investigation could be pursued. We had no authority to make any physical

examinations or anything of that kind, our conclusions being based on occasional conversations and statements of the men.

The consensus of opinion among the laboring men seems to be that work in the Subway is no worse than work anywhere else.

The conductors and motormen do not mind it because only a comparatively small part of each trip is spent in the tunnel.

The station men, ticket agents, and others, who remain in the Subway practically all day, complain of "colds," rheumatism, dampness, and lack of sunlight. That the effect of this life underground would in the long run be detrimental to the health of the individual goes without saying.

As for the passenger who rides once or twice a day for a few minutes through the Subway—taking into consideration every factor that goes to make up the sanitary condition of a structure of this kind—we would unhesitatingly say that he is better off than in a surface car.

To briefly review our results, we will conclude with the following summary:

The Subway temperature is higher than outside in cold weather and lower than outside in warm weather. The difference is more marked in cold weather, on clear days, and in the event of a sudden change of outside temperature.

We found the ventilation to be ample, it being possible to change the entire air content of the tunnel in an hour and fifteen minutes.

For consideration of air currents due to movements of cars see p. 190.

In cold weather the relative humidity was generally higher outside the Subway. In hot weather the reverse held true. The average relative humidity in the subway remained about 64 per cent. in both hot and cold weather.

The dust count was higher in the Subway during the winter months. In warm weather it was higher in the street.

The carbonic acid averaged 4.8 parts per 10,000 outside and 6.5 parts per 10,000 inside the Subway.

The common air organisms were found in great abundance, together with numerous molds. No pathogenic bacteria were found.

The above charts, tables, and conclusions are based upon over 4000 observations which we have had the pleasure of making in the Market Street Subway during the past six months.

Grateful acknowledgment is due to Dr. Abbott, through whom permission was obtained from the Philadelphia Rapid Transit Company to enter the Subway.

We wish also to acknowledge our indebtedness to Dr. Bergey for daily advice and suggestions in regard to the work.

To Mr. John E. Walt and Mr. Thomas J. Barry our thanks are due for assistance in obtaining convenient points for comparative outside observations.

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THE DISTRIBUTION OF THE MOTOR ROOT IN THE ANTERIOR HORN.

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In a short but comprehensive paper by Blumenau and Nielsen[1] the relation of the posterolateral cell groups of the anterior horn of the fifth, sixth, seventh, and eighth cervical and first thoracic segments of the spinal cord to the muscles of the shoulder is exploited. Mention is made of experimental work on animals along these lines by Marinesco,[2] M. and Mme. Parhon,[3] and De Neef[4] and a similarity of cell-group functions between man and the lower animals is shown.

The case I am reporting has already been made the subject of a study in another line by Spiller,[5] to whom I am indebted for the pathological material.

A patient denying specific disease and having suffered from severe left frontal headache for two years began to show signs of brain tumor, viz., motor aphasia, weakness of right arm and hand, partial paralysis of right side of face, and convulsive seizures in which consciousness was not lost. "A diagnosis of tumor of the lower left motor area was made. It was supposed to affect Broca's area by pressure or to invade it slightly, inasmuch as the motor aphasia was incomplete." At the operation (performed by Dr. C. H. Frazier) the tumor was exposed, and because of the extent and vascularity no attempt was made to remove it in its entirety. The tumor grew rapidly after the operation, and the patient died about twelve weeks later. At the necropsy "a tumor was found in the posterior part of the left second frontal convolution extending into the middle of the precentral convolution and to the upper part of Broca's area. The growth was infiltrating and at no part sharply defined from the surrounding tissue. It was, as already said, a small spindle-celled sarcoma."

Upon opening the spinal dura there was found a small tumor involving the right sixth cervical anterior nerve root. This is well demonstrated in the picture (Fig. 1), where is also seen a fasciculus at the lower border of the segment escaping the neoplasm and entering the spinal cord without interference. This growth was entirely unsuspected owing to the masking of any possible symptoms by the partial hemaplegia. Microscopic study shows this small tumor to be a fibrosarcoma.

Serial sections were made throughout the upper part of the sixth segment and one in every five was stained by von Lenhossék's method (thioninphenique).

In describing the changes found in the anterior cornual cells I shall follow the grouping as accepted in the work of F. Sano.[6]

In referring the cell groups of this study to the classification adopted by Sano, I do so because his diagram (p. 32 of the original article) so perfectly illustrates the groups of cells degenerated; but the verity of his conclusions I am in no position to affirm or deny.

The number of cells in each anterior horn was counted, great care being taken not to know which horn was under consideration until after the count for that section was completed. This precaution was taken in order to obliterate as much as possible "the personal equation." The sections are numbered from above downward and the figures are arranged in the following table:

No. of slide.	Right.	Left.	Difference.
5	34	54	20
10	16	29	13
15	35	44	9
20	21	37	16
25	19	45	26
30	29	33	4
35	32	35	3
40	37	49	12
45	25	40	15
50	33	50	17
55	34	51	17
60	41	53	12
65	31	48	17
70	34	55	21
75	38	41	3
80	40	47	7
85	23	33	10
90	52	45	*7
95	32	35	3
100	37	39	2
105	30	36	6
110	38	42	4
115	44	38	*6
120	46	35	*11
125	33	40	7
	834	1054	220

In every section, with the exception of Nos. 90, 115, and 120, there are fewer cells in the right anterior horn than in the left. The greatest differences are encountered in the upper part of the segment. The three exceptions above noted are in the lower part of the tissue examined where the horns are more equal in count, and asterisks are placed in the fourth column indicating these exceptions.

It must be remembered that a small fasciculus of fibers, the lowest in the root, escaped involvement in the tumor mass, and this accounts for the discrepancy in count being less the lower down the section.

Directly opposite the entrance of the nerve root the anterior cornual cells show a marked degeneration in that group which Sano designates as the group for the serratus magnus. This collection of cells is, in this segment, the most anterior group, and is numbered in Sano's diagram "4." (This diagram has been reproduced in M. Allen Starr's *Organic Nervous Diseases.*)

The sections, as we pass upward, show a change in the locality of the degenerated cells, the anterior Group "4" clearing up and becoming normal as the two groups on either side of and very slightly posterior to it present positive, though not very pronounced, signs of degeneration. Sano indicates these two groups as follows: That on the outside of Group "4" he numbers Group "6," and designates its sphere of activity as the shoulder muscles; that on the inside he calls Group "1" and ascribes to it the innervation of the extensors and rotators of the vertebral column.

The clearing up of the degeneration in Group "4" as we proceed downward is not followed by such pronounced signs of involvement of the two groups, on either side of and posterior to it, as is the case in the upper part of the segment. But, nevertheless, there is the same tendency for the involvement of the group to the outer side, called Group "7," to which is ascribed the innervation of the flexors and pronators, and the group on the inner side which is a continuation of the original Group "1."

By way of a conclusion I offer the accompanying diagram as a possible distribution of the fibers of the sixth cervical anterior nerve root (Fig. 2).

FIG. 1.—Spinal cord showing small tumor involving the greater part of the right anterior nerve root of the sixth cervical segment.

According to this scheme the ultimate destination of the axones of cells in Group "4" below and above the degenerated area is unaccounted for, as is also the middle areas of the mesial and lateral columns.

In a case of brain tumor, where the character of the neoplasm is such that metastasis may occur, it is well to realize how completely spinal symptoms, due to a metastatic growth, may be masked by the hemiplegia present. Should a tumor involve only the anterior root, it is entirely conceivable

that no symptoms would be detected even though the patient had no masking hemiplegia. If, for instance, the sixth cervical anterior nerve root on the right were cut or destroyed by any lesion, there is no muscle which would not still have representation in segments above or below this, with the possible exception of the pronator radii teres and the flexor carpi radialis.

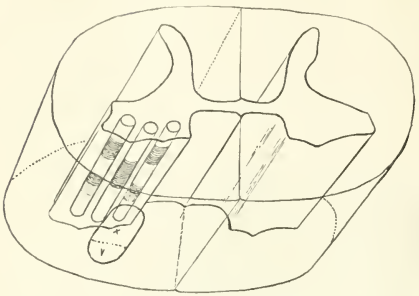

Fig. 2.—A scheme representing a possible distribution of the fibers of the anterior nerve root in the anterior horn of gray matter (the shaded and dotted area). *X*, in the oval, represents the part of the root invaded by the tumor; *Y* represents that part of the root free from tumor. The shaded portions of the three columns represent the locality of the degenerated nerve cells.

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REGENERATION OF BONE.

An Essay, Illustrated by Photographs and Photomicrographs, Dealing with the Repair of Simple Fractures and the Regeneration of Bone after Partial Injury and Subperiosteal Resection.

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(Concluded from page 183.)

SERIES 7.

This series, upon dogs, was performed with the object of determining whether an animal substance placed under the periosteum would cause the formation of bone when not associated with injury to the bone. Each operation consisted in making an incision over the tibia to the bone. A longitudinal incision was then made along the side of the bone and the periosteum was raised up. A coil of catgut, No. 2, was placed under it and the wound closed with silk and covered with collodion.

Experiment 69. Operation performed June 7, 1906. Animal killed July 12, 1906. Fracture of thirty-five days' duration.

Macroscopic Description. The wound had united by first ntention. Removal of the skin revealed the fact that the catgut remained unabsorbed. No callus or new bone could be noticed. Section through the bone showed the periosteum to be greatly thickened and the unabsorbed catgut to be encapsulated. There was no apparent new-bone formation. The medulla was red in the upper half of the section and yellow in the lower. In the medullary cavity there was no callus or new-bone formation.

Microscopic Description. The catgut is encapsulated, with slight absorption taking place by the action of leukocytes, which are rather abundant. The encapsulating tissue consists of fibroblasts with large vesicular nuclei. At one place, where the periosteum is still attached to the bone, there is a thin deposit of dense osteoid tissue which exhibits slight absorption. The trabeculæ are not covered by osteoblasts. There is superficial absorption of the cortex by osteoclasts.

In the cortex proper, near the periosteal surface, there is some absorption with widening of a few of the Haversian spaces. These are lined by osteoclasts. The medulla shows increased cellular content on the edges. No osteoclasts or trabeculæ are present.

Experiment 70. Operation performed May 29, 1906. Animal killed July 19, 1906. Fracture of fifty-one days' duration.

Macroscopic Description. The wound had healed completely without suppuration. On removing the skin, the catgut was found coiled up as when it had originally been placed under the periosteum and no absorption was apparent. The catgut was adherent but the periosteum was not thickened and there did not appear to be any new-bone formation. Longitudinal section showed no new-bone formation, but the entire marrow was of the red variety. No microscopic sections were made owing to the fact that the gross specimen was mislaid.

SERIES 8.

This series, upon dogs, was performed with the object of determining whether an unabsorbable substance placed under the periosteum would excite the formation of bone when not accompanied by injury to the cortex.

The operations were similar to the preceding one, with the exception that celloidin, hardened in bichloride alcohol, was placed under the periosteum instead of catgut. In this series, as in the two series following, there is but one successful operation.

Experiment 71. Operation performed May 29, 1906. Animal killed July 19, 1906 Fracture of fifty-one days' duration.

Macroscopic Description. The wound had united perfectly without suppuration. No thickening could be felt at the site of the operation. On removing the skin the celloidin was found still in the place where it had been put, but dried out and brown in color. It was not encapsulated and the periosteum did not appear to be thickened. There was no visible bone formation.

Longitudinal section confirmed the above. The medulla was red throughout the bone.

Microscopic Description. The celloidin still remains, but it appears as if it had slipped out from under the periosteum, as there is periosteum between it and the bone. There is an apparent effort at encapsulating the celloidin, a layer of fibroblasts and leukocytes being around it. The periosteum shows proliferation in its deeper surface and there is superficial absorption of the cortex by osteoclasts. There is no sign of trabeculæ formation. The cortex proper has undergone no absorption. The medulla is red and contains osteoclasts.

SERIES 9.

This operation was performed with the object of determining the influence of a blood clot underneath the periosteum when not associated with injury to the bone itself. It consisted in making an incision over the radius to the bone and raising the periosteum. The periosteum was very thin and it was difficult to elevate it. The wound was then sutured without any effort having been made at hemostasis in the deeper parts of the wound.

Experiment 72. Operation performed June 7, 1906. Animal killed July 19, 1906. Fracture of forty-two days duration.

Macroscopic Description. The wound had healed completely without suppuration. On removing the skin there was found a small, discolored area under the wound in the soft tissues, but no evidence of the operation upon the bone could be found.

Longitudinal section failed to reveal any evidence of the operation.

Microscopic Description. There is superficial lacunar absorption of the cortex by osteoclasts, where the periosteum had been raised. There is no attempt at trabeculæ formation. The deeper layer of the periosteum exhibits some cellular proliferation, the superficial layer still being fibrous. The cortex proper shows no absorption whatever. The marrow is red in both the injured and uninjured bone, and there are osteoclasts throughout its entire substance.

SERIES 10.

This operation was performed with the object of determining the effect upon bone production of merely raising the periosteum and letting it immediately fall back into place. An attempt at perfect hemostasis was made. The operation was similar to Experiment No. 72 in every other respect.

Experiment 73. Operation performed June 7, 1906. Animal killed July 19, 1906. Fracture of forty-two days' duration.

Macroscopic Description. The wound had healed completely without suppuration. On removing the skin there was found a small patch of discoloration under the wound in the soft tissue, but there was no evidence of the operation upon the bone. Longitudinal section through the bone failed to reveal anything further.

Microscopic Description. There is superficial absorption of the cortex by osteoclasts and proliferation of the deeper layers of the periosteum, with no attempt at trabeculæ formation. The unoperated bone, also, shows slight absorption of its surface, but to a very minor degree. In the cortex there are several dilated spaces caused by absorption by osteoclasts. These spaces are lined by osteoclasts. The marrow of both bones is red and shows osteoclasts.

SERIES 11.

This series consisted of two operations upon dogs and had as its object to determine whether a subperiosteal resection, when not in the presence of infection, would be followed by complete regeneration of the bone. This series did not consist of a simple complete subperiosteal resection, but differed in that a thin strip of bone was left remaining in order to see if it would hasten the regeneration by allowing a framework upon which to build.

Each operation was performed by making an incision over the tibia to the bone, and then a longitudinal incision through the periosteum for about two inches. The periosteum was raised from the bone for almost the entire circumference and then retracted, while two sawcuts, about an inch apart, were made half-way through the bone. The intervening portion of the cortex was grasped between the jaws of a bone forceps and a lid taken off the medullary cavity between the two cuts. The remainder of the bone intervening was removed piecemeal by bone forceps, with the exception of a thin strip next to the fibula. The cut ends of the tibia were bevelled off as much as possible to avoid leaving a dead space when the periosteum was sewed up. The periosteum was then sutured throughout the entire length of the incision in it, so that the two inner surfaces were in contact. Chromicized catgut was used for the purpose. The skin was also sutured with a buttonhole suture of chromicized catgut and the leg wrapped in a wet bichloride dressing. Finally, the leg was placed in a shaped splint, which was retained in position with a sodium silicate dressing.

Experiment 74. Operation performed November 19, 1906. Animal killed January 5, 1907. Fracture of forty-seven days' duration.

Macroscopic Description. The wound had healed perfectly and the leg was firm. There was no catgut remaining. A large nodular callus filled in the defect in the tibia. It appeared as if there had been a fracture of the fibula that had reunited.

Radiograph (Fig. 28). The *x*-rays reveal the fact that the fibula and the remaining strip of tibia had evidently been fractured, but the position of the fragments had remained good and there is no apparent shortening. The areas from which the cortex had been removed are still visible. There is what appears to be a small deposit of osteoid tissue on one fragment.

Longitudinal section through the bone confirms the *x*-rays in that a fracture of the fibula with callus was found. The defect in the tibia was filled with cartilage, with a small amount of osteoid tissue at the ends of the cortex of both fragments.

Microscopic Description. The sections confirm the *x*-rays and gross findings. The fibula is fractured and the site of fracture is surrounded by a spindle-shaped callus of osteoid tissue, with a wide band of fibrocartilage across the line of fracture. The portion of the tibia from which the cortex and medulla have been removed is filled with a dense fibrocartilage. The parts of the cartilage nearest the ends of the fragments appear more hyaline, the cells becoming larger and the intercellular substance less fibrillated. The cells arrange themselves in rows resembling the epiphysis of a growing bone. The ground substance between these rows is absorbed and vascularized. This is followed by a deposition of calcium salts and the formation of osteoid trabeculæ over the exposed medullary ends of the fragments. Between the trabeculæ are large, thin-walled bloodvessels.

The old cortex has undergone considerable absorption, especially at the operated ends, where the lacunar osteoclastic absorption is distinctly evident. The medulla is somewhat cellular, but many fat cells remain.

Experiment 75. Operation performed November 22, 1906. Animal killed January 5 1907. Fracture of forty-four days' duration.

Macroscopic Description. The wound was healed perfectly. On removing the skin all signs of the catgut had disappeared. The leg was firm, the animal having had use of it. A large nodular callus filled in the interval where the bone had been removed from the tibia. This callus was thicker than the original bone.

Radiograph (Fig. 29). *X*-rays reveal the fact that the fibula had remained unbroken, but the strip of tibia that had been left remaining had been fractured, but was retained in perfect position. This strip of old cortex is covered with new-bone formation. This deposit does not fill in the entire defect in the tibia, but is only about one-eighth inch thick at its thickest portion. There is still another deposit of osteoid tissue separated from this mass in the form of an island between the two fragments of bone. The remainder of the defect must be filled in with cellular material, as it appears in the picture as a mere haze.

Longitudinal section confirms the *x*-rays completely and shows that the material filling in the defect is cartilage with the exception of the osteoid tissue before mentioned.

Microscopic Description. The fibula is intact, but has a deposit of osteoid tissue upon its tibial aspect for almost the entire length of the bone.

The defect in the tibia is filled by cartilage and osteoid tissue. The osteoid trabeculæ are along the bridge of old bone left remaining between the two fragments, across the ends of the bone and in the form of a small island in the cartilage filling in the remainder of the defect. The cartilage is more fibrous in nature than hyaline. At its edges the cells have a tendency to arrange themselves in rows, but to a lesser degree than in the last experiment.

The osteoid trabeculæ, as in most of the following experiments, appear to be composed of very delicate trabec-

ulæ caused by direct transformation of cartilage by a deposition of calcium salts. These form the interstitial bone and take a bluish stain. Upon the surface of these there is a deposit of new bone which is much denser in appearance and takes a deep-red stain with eosin. This tissue has a distinct lamellar arrangement and resembles osseous tissue, forming Haversian canals and systems.

The cortex has undergone great absorption, with a deposition of new bone in the widened spaces. There is lacunar absorption of the ends of the bone. The marrow does not appear to be very cellular.

SERIES 12.

This series, upon dogs, was performed with the object of determining if there would be regeneration of bone after a complete subperiosteal resection when not in the presence of inflammation. There were two operations in this series and each was identical with the previous two, with the exception that there was no bridge of cortex left, but the entire section of bone removed and the periosteum then sutured as before.

Experiment 76. Operation performed November 26, 1906. Animal killed January 11, 1907. Fracture of forty-six days' duration.

Macroscopic Description. The wound had healed by first intention. There was some rocking mobility and it appeared as if the fibula had been fractured, as there was some callus in that region. The catgut was still present, but encapsulated. There was some thickening in the region of the operation, but there did not appear to be regeneration of the bone.

Radiograph (Fig. 30). *X*-rays reveal the fact that the fibula had been broken and that there was lateral deviation of one of the fragments of the tibia. There appears to be a slight new-bone formation at the ends of the tibia, but none whatever in the space where the cortex had been removed. There is some osteoid callus at the site of the fracture of the fibula.

Longitudinal section was very unsatisfactory, not having gone through the centre of the bone, so that no conclusions could be drawn from it.

Microscopic Description. The fibula is not to be found owing to the direction of the sections and the half of the bone chosen for section. The area from which the cortex had been removed is filled in greater part by very dense connective tissue with fibrocartilage near the ends of the tibia. The medullary cavities of the exposed ends are covered in with a very thin layer of osteoid tissue. There is also a small nodule on the fibular aspect of the periosteal side of one of the fragments. A rather large island of osteoid tissue is on the fibular side of the space from which the bone had been removed. This is probably a portion of the callus of the fractured fibula.

The callus present is undergoing absorption principally by leukocytes.

The cortex is greatly rarefied and the ends of the fragments exhibit extensive lacunar absorption by osteoclasts. The marrow is rather cellular.

Experiment 77. Operation performed November 28, 1906. Animal killed January 11, 1907. Fracture of forty-four days' duration.

Macroscopic Description. The wound had healed perfectly. The leg was quite firm, but there was some rocking motion to be felt at the site of the operation. The catgut was still present and encapsulated. The defect in the tibia was filled in comparatively well and was rather firm, but not bony.

Radiograph (Fig. 31). *X*-rays reveal the fact that the fibula had been fractured and was in quite good position at the time the picture was taken. There is a moderate amount of callus thrown out around the site of the fracture. The tibia has shortened, closing in the space between the ends of the bone and obliterating the defect excepting where the bone is bevelled off. There is no new bone where the old had been removed.

On the bevelled surface of one fragment there is a very thin deposit of new bone.

On longitudinal section the fibula was shown to have been fractured. There was a comparatively large callus thrown out around the line of fracture. The defect in the tibia was still present and did not appear to be filled in with anything but fibrous tissue, which was not very dense. On the periosteal surface of the ends of the fragments there was some spongy bone formation, and there was also a thin shell of osteoid bone formation over the ends of the medullary cavities. The marrow was red in color.

Microscopic Description. The sections confirm the *x*-ray and gross findings. The defect was filled in with rather cellular fibrous tissue. There is an osteoid nodule from the fibular callus which is surrounded by fibrocartilage. The medullary cavities of the ends of the fragments of the tibia are covered by osteoid trabeculæ which are undergoing lacunar absorption in areas. The spaces between them are filled with very cellular marrow. The cortex is riddled with dilated Haversian spaces. The catgut can be seen undergoing absorption.

SERIES 13.

This series, consisting of two operations upon dogs, was performed with the object of determining if the placing of medullary tissue between the two surfaces of the periosteum, after removing the cortex, would influence the regeneration of the bone. The operations were identical with those of the previous series, with the following exception. When the lid of the cortex was removed from between the

two sawcuts, the medulla was removed intact and placed in normal salt solution while the remainder of the cortex was being removed.

It was then placed between the two layers of periosteum before they were sutured together.

Experiment 78. Operation performed December 26, 1906. Animal killed January 26, 1907. Fracture of thirty-one days' duration.

Macroscopic Description. The wound had united by first intention. On removing the skin the catgut was found to have been absorbed with the exception of the knot. The leg was in good alignment and quite firm A very slight amount of rocking could be elicited but no mobility at the site of operation.

Radiograph (Fig. 34). Unfortunately the picture was not taken at quite the right angle, so that the tibia is partially in front of the fibula, but, nevertheless, every point is distinct. The fibula is seen to be intact and there is no shortening of the tibia, the ends of the fragments remaining separated as at the time of the operation. There is a bridge of osteoid tissue extending from one fragment to the other, the thickness of which cannot be determined because of the angle of the picture.

Longitudinal section confirmed the radiograph. The defect was filled with cartilage containing islands of rather dense bone; also more spongy bone. The marrow of the ends of the fragments was red, but the medullary cavities did not appear to contain much new-bone formation with the exception of the ends, which were closed in by it. The periosteal aspect did not seem to have any new-bone formation upon it.

Microscopic Description. The fibula is intact and has upon its periosteal surface a deposit of new bone. The cortex is greatly rarefied.

The defect in the tibia is filled in with irregular masses of hyaline and fibrocartilage, osteoid tissue, and dense fibrous tissue. The osteoid tissue is quite abundant. Its marrow spaces are very large and filled with cellular red marrow and red blood cells. The cartilage is mostly of the very cellular hyaline variety, taking a deep-blue hematoxylin stain. There is also some fibrocartilage and dense fibrous tissue which is becoming riddled by bloodvessels. The old cortex shows great absorption. The marrow is somewhat cellular, and, extending across the medullary cavity at the ends of the fragments, there are bridges of osteoid trabeculæ.

Experiment 79. Operation performed November 30, 1906. Animal killed January 21, 1907. Fracture of fifty-two days' duration.

Macroscopic Description. The wound had healed by first intention. The leg was perfectly firm and solidly united without a depression at the site of operation. On removing the skin the catgut was found to have been absorbed, and there was a slight elevation at the site of the original defect in the tibia.

Radiograph (Fig. 35). This is very interesting and in marked contrast to those of the other series. The fibula is seen to be intact and the distance between the ends of the tibia about the same as at the time of operation. The defect in the tibia is more than refilled with new-bone formation, which is continuous from one fragment to the other and wider than the normal width of the bone. It shows some light streaks through the mass, due probably to islands of cartilage.

Longitudinal section through the bone confirmed the radiograph in all respects. The new bone was found to be vascular, red, spongy bone. It was broken into large islands by the interposition of narrow islands of cartilage. The marrow of both fragments was red and hyperplastic, but there did not appear to be a great amount of new-bone formation in either of the ends of the bone.

Microscopic Description. The fibula is intact, but has shared in the general regenerative process, and the cortex has undergone considerable rarefaction. Its periosteum has proliferated and osteoblasts are present in abundance.

The defect in the tibia is filled in completely by osteoid tissue and cartilage. The trabeculæ are arranged in irregular anastomosing masses with cellular hyaline cartilage, taking a deep-blue hematoxylin stain on the outskirts. Between the masses are slits or spaces lined on both sides by cartilage, probably due to the fact that the masses began as separate islands of cartilage which grew until they were in apposition with each other, but not united. The spaces between the osteoid trabeculæ are quite large and filled with very cellular red marrow and red blood cells. The trabeculæ are covered with osteoblasts, and there are a great number of very large osteoclasts present, causing absorption in other areas. The old cortex is riddled with dilated Haversian spaces. The marrow is cellular toward the ends of the fragments and contains the variously sized cells, etc., described under several previous experiments. Near the site of the operation it contains numerous multinuclear cells indistinguishable from osteoclasts. The trabeculæ are composed of osteoid tissue, evidently due to calcification of the old cartilage, on which have been deposited several lamellæ of osseous tissue, taking a deep eosin staining.

SERIES 14.

This series consisted of two operations upon dogs with the object of determining whether or not placing dried bone chips between the two layers of the periosteum, after removing the cortex, would hasten the regeneration of the bone. The operations were identical with those of Series 12, with the exception that before sewing the periosteum, thin slices of bone that had been ground and the balsam

removed were placed between the two layers of periosteum and sewed there.

Experiment 80 Operation performed December 28, 1906. Animal killed January 5, 1907. Fracture of eight days' duration.

Macroscopic Description. The wound was healed and the sutures were still in place. The sections of bone placed between the layers were still there and surrounded by blood clot.

Radiograph (Fig. 32). *X*-rays reveal the fact that the fibula was not fractured and that there was no shortening of the space between the ends of the tibia. Slight evidences of the thin strips of bone that had been placed between the layers of the periosteum, can be seen, but they do not come out as plainly in the prints as they do in the negative. There is no apparent growth of new bone anywhere.

Longitudinal section demonstrated that the defect in the bone was filled with firm blood clot and that the medulla of the ends of the fragments was firm and condensed. It was red in color.

Microscopic Description. The fibula is not fractured, but is rarefied and has a deposit of osteoid tissue upon its periosteal surface. In the centre the defect in the tibia is filled with blood clot. Toward the ends of the fragments of the tibia it is replaced by loose connective tissue. Throughout this tissue, which appears to take origin from the medulla, are numerous round or oval cells with round, well-staining nuclei, and a considerable amount of protoplasm. These cells resemble closely the normal marrow cells. The tissue is quite vascular.

The marrow of both fragments exhibits considerable connective-tissue hyperplasia and contains abundant, thin-walled, engorged bloodvessels, which are streaming into the tissue filling the defect in the bone. The cortex has undergone extensive absorption, especially at the ends. There are abundant osteoid trabeculæ on the periosteal surface, also in the medullary cavity near the ends and over the ends of the cortex itself. The catgut is still plainly visible, encapsulated by connective tissue and leukocytes, not having undergone absorption.

Portions of the strips of bone placed between the layers of periosteum can be seen. Some of them appear to be undergoing lacunar absorption. There is no deposit of new bone on the surface, as was seen in many of the experiments where the splinter of bone had been broken off at the time of the operation.

Experiment 81. Operation performed December 28, 1906. Animal killed January 26, 1907. Fracture of twenty-nine days' duration.

Macroscopic Description. The wound had united, but the fibula was fractured and there was no attempt whatever at union. A large nodule could be felt over the fibula. The catgut remained unabsorbed and the defect in the tibia showed no evidence of new-bone formation.

Radiograph (Fig. 33). *X*-rays reveal the fact that there was a fracture of the fibula, with angular displacement and non-union. Callus can be seen above and below the site of fracture of the fibula. The space in the tibia from which the bone had been removed has collapsed. There is no apparent new-bone formation in it and no signs of the piece of bone placed between the layers of the periosteum.

Longitudinal section confirmed the *x*-ray findings. The defect in the tibia was as when it was made with the exception that the alignment of the tibia had changed by displacement and this reduced the length of the defect. It was filled in with soft connective tissue. No bone or cartilage was to be seen. Along the sides of the medullary cavity of the ends of the fragments there was some new-bone formation and also on the periosteal surface. The medulla was pink in color.

Microscopic Description. The fibula is fractured and there is considerable callus in the region of the fracture, upon both fragments, with cartilage across the line of fracture.

The defect in the tibia is filled with loose, vascular, cellular connective tissue. But few osteoid trabeculæ are present, these being upon the fragments of the tibia. There are no signs of the section of bone placed between the layers of the periosteum. There is considerable absorption of the cortex of both fragments, interstitially and at the ends. The marrow is somewhat hyperplastic.

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BOOK REVIEWS.

PRACTICAL PHYSIOLOGICAL CHEMISTRY. A BOOK DESIGNED FOR USE IN COURSES IN PRACTICAL CHEMISTRY IN SCHOOLS OF MEDICINE AND OF SCIENCE. By PHILIP B. HAWK, M.S., PH.D., Demonstrator of Physiological Chemistry in the Department of Medicine of the University of Pennsylvania. Philadelphia: P. Blakiston's Son & Co.

The author intends this work solely as a manual for students. As such it appears to be one of the best of which we have any knowledge. Many books with the same purpose consist too much of a series of laboratory directions, interpolated with questions to the student answered in the text. The writer here has preserved to a degree this element, in order to stimulate the student to think for himself, but he has also given a background of valuable reference matter which leads logically to the more characteristic reactions of the subject under discussion. These the reader is meant to work out for himself.

The work is broad in its scope and thoroughly up to date. It presupposes a fair working knowledge of organic chemistry, but gives a good bird's-eye view of the various fields of physiological chemistry.

It is really of somewhat wider value than a student's manual and it is a pity that the author has sometimes sacrificed valuable data, incidental to the text, to the propounding of questions which the student is meant to answer through his own efforts. In conjunction with the abundance of useful material contained, more complete data would add much to the general utility of the work and commend it as a reference hand-book for the laboratory, alike to students and others. For example, he gives fairly complete directions for the quantitative determination of uric acid by several methods, but omits stating anywhere the melting point of urea, though he devotes a paragraph to it, meaning the student to discover this through suitable experiments.

The author eminently fulfils his own purpose, however; his style is clear and simple; the illustrations of the text are abundant and there occur such references as will enable the reader to recognize differences of opinion and become familiar with the authorities quoted.

As a laboratory manual for colleges, the book should be widely acceptable, especially as such works are rarer in this country than abroad, and there are many reasons why an English text is preferable to a German translation. R. P.

THE NEW HYGIENE. THREE LECTURES ON THE PREVENTION OF INFECTIOUS DISEASES. By ELIE METCHNIKOFF, with Preface by E. RAY LANKESTER. Chicago: W. T. Keener & Co., 1906.

These lectures given as the Harben Lectures by Metchnikoff embody many of his theories and conclusions reached after twenty-five years of thought and study. They are in a form easily understood by anyone with a small amount of medical knowledge, and contain much of interest to those studying deeper medical problems. The first lecture on Hygiene of the Tissues is devoted to a discussion of the theory of immunity in which the author places special emphasis on phagocytosis, while the opsonic influence is looked on as quite subordinate. The actions of alcohol in diminishing and of horse serum in increasing immunity to infection depends, according to the author, on the harmful action of the one and the stimulating action of the other on the phagocytes.

The second lecture on the Hygiene of the Alimentary Canal deals with the phagocytosis of food and pathogenic microörganisms from the intestinal canal and discusses at some length the etiology of appendicitis. In this latter connection the author offers the rather unique explanation that many cases of appendicitis are due to the presence in the appendix of intestinal parasites which either by their presence or by their bites permit infection of the mucous membrane by pathogenic organisms. So firm is his belief in this theory that he advises the administration of thymol in all cases of the disease irrespective of whether or not the ova of parasites are found in the intestinal discharges.

The third lecture discusses the Hygienic Measures Against Syphilis. The author sets aside as impracticable in lessening the spread of the disease such measures as early marriages, regulation or abolitionism of venereal diseases, and gives in some detail the evidence which has led him to believe that certain monkeys, chiefly the macaci, may attenuate the syphilitic virus, an observation which may later lead to a practical method of antisyphilitic vaccination. The lectures cannot help but be of interest to both the layman and the physician, and they contain many original theories and ideas of decided interest in connection with the present rather unsettled and complicated question of immunity and its application to human health. F. H. K.

A TEXT-BOOK OF OBSTETRICS. By BARTON COOKE HIRST, M.D., Professor of Obstetrics in the University of Pennsylvania. Fifth revised edition. Octavo of 915 pages, with 753 illustrations, 39 of them in colors. Philadelphia and London: W. B. Saunders Co., 1906.

This work continues to occupy the position it originally attained—that of one of our standard texts on Obstetrics. The style and arrangement are especially noteworthy as applicable to the use of students and general practitioners. In this, its fifth edition, the revision has been chiefly in the chapters dealing with puerperal infection and the toxemias of pregnancy. Some new illustrations have been scattered throughout the book. These, though not particularly artistic, present admirably the point they are intended to emphasize. For this reason, the number of diagrams, which always eluci-

date so much more distinctly than photographs and filled-in drawings, are to be commended.

The various methods of inducing labor and of rapidly terminating labor, particularly when the cervix is rigid—the choice of which is now being so extensively discussed in the literature—is not very largely entered into. Vaginal Cesarean section is not very fully described, nor are its indications and especially its contra-indications given. Pubiotomy, which seems to be supplanting symphyseotomy in the hands of some authorities, is not mentioned. These shortcomings are perhaps rather to be praised than condemned in a book which is intended for students and general practitioners for whom these operations are undoubtedly too major. In the chapter on puerperal sepsis methods of precision in diagnosis, as intra-uterine and blood cultures, are fully considered.

On the whole the work is an excellent one. Its chief fault is its brevity especially in dealing with some of the less frequent pathological conditions complicating pregnancy and the puerperium. A work of greater magnitude from the pen of a man with the experience of this author would indeed be interesting and useful. J. W. L.

Blood Serum Therapy. By Walter Jowett, F.R.V.S., D.V.H., Formerly Demonstrator of Comparative Pathology and Bacteriology in the University of Liverpool. Chicago: W. T. Keener & Co.

This recent work, published for veterinary practitioners and students, as mentioned by the writer, gives a short account of the subject of immunity and of the vaccines, sera, and toxins used in present day veterinary practice. The work is well divided under five chapters, namely:

Chapter I. Immunity. In which the well-known theories explaining immunity are brought out in a clear and concise form.

Chapter II. The Methods of Conferring Immunity. Explains in detail what is meant by active and passive immunity and the treatment by vaccines and serum therapy of the well-known bacterial diseases of the lower animals. The diseases due to the organisms generally classified under the hemorrhagic septicemia group are given the name Pasteurelloses by the writer, the treatment of which, by polyvalent vaccines and sera, is upheld in a very positive manner, this being open to criticism.

Chapter III. Diseases Due to Ultravisible Viruses. The chapter is well given over in describing the principles underlying the preventive treatment of rabies, variola, cow-pox, foot and mouth disease, etc.

Chapter IV. Diseases Due to Protozoa. In this chapter, stress is laid upon the methods at hand in the establishment of immunity in the piroplasmic diseases, as Texas fever. Short mention is made of the absolute failure to obtain immunity in the experiments with the trypanosomata.

Chapter V. Toxins and Serum Diagnosis. The chapter is limited to the making and use of tuberculin and mallein, with details regarding their use. An outline of the principles of serum diagnosis, with special reference to the glanders agglutination test, takes up the remainder of the chapter.

J. R.

UNIVERSITY OF PENNSYLVANIA

DEPARTMENT OF MEDICINE

FOUNDED IN 1765

This Medical School, the oldest in the United States, was founded in 1765 by Dr. John Morgan, who filled in it the first medical professorship created in America. In his opening "Discourse upon the Institution of Medical Schools in America," delivered in the College of Philadelphia on May 30, 1765, Dr. Morgan uttered these prophetic words: "Perhaps this medical institution, the first of its kind in America, though small in its beginning, may receive a constant increase of strength, and annually exert new vigor. It may collect a number of young persons, of more than ordinary abilities, and so improve their knowledge as to spread its reputation to distant parts. By sending these abroad duly qualified, or by exciting an emulation amongst men of parts and literature, it may give birth to other useful institutions of a similar nature, or occasional rise, by its example to numerous societies of different kinds, calculated to spread the light of knowledge through the whole American continent, wherever inhabited."

Through Dr. Morgan, the pupil of Hunter in London and of Cullen in Edinburgh, the graduates of this school take a just pride in regarding it as the lineal descendant of the best medical schools of Great Britain in the last century. To Dr. Morgan was soon joined another pupil of Cullen, Dr. William Shippen, as Professor of Anatomy and Surgery, thus forming another tie of relationship to the celebrated University of Edinburgh, whose methods of instruction were substantially adopted here. In the next year Dr. Adam Kuhn was added as Professor of Botany and Materia Medica; and in June, 1768, a "Commencement was held," at which medical honors were bestowed, the first in point of time in America. In 1769, Dr. Benjamin Rush was elected Professor of Chemistry, while Dr. Thomas Bond, one of the trustees of the College of Philadelphia, delivered lectures on Clinical Medicine in the Pennsylvania Hospital.

To the faculty thus composed of Morgan, Shippen, Bond, Kuhn, and Rush have succeeded, at various times, professors whose reputation has been national, such as Wistar, Barton, Physick, Chapman, Hare, Gibson Horner, Dewees, Jackson, George B. Wood, Hodge, James B. Rogers, Carson, R. E. Rogers, Leidy, Henry H. Smith, Pepper, Francis Gurney Smith, Stillé, D. Hayes Agnew, Goodell, W. Pepper, Jr., and Ashhurst.

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The University has decided to make important additions to the requirements for admission; some of these additions will be required in 1908, others in 1909, and still others in 1910.

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For 1909–1910, in addition to the requirements for 1908–1909, as above described, the successful completion of work equivalent to that prescribed for the Freshman Class, in a college recognized by this University.

For 1910–1911, in addition to the requirements for 1909–1910, as above described, the successful completion of work equivalent to that prescribed for the Freshman and Sophomore Classes in a college recognized by this University.

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UNIVERSITY OF PENNSYLVANIA MEDICAL BULLETIN.

ADDRESS BY ALLEN J. SMITH, M.D.

Opening Address in Medical Department of the University of Pennsylvania. Session of 1907-08.

Some years ago—it is nearly a generation in the past, I regret to say, with due remembrance of the sweep of time and the remorseless fate of man—William Osler, whose portrait hangs above us, delivered at one of the Commencement exercises of this school an address entitled "Equanimitas," which has since been published as the title-chapter of his little book of the same name—in which he developed as his theme the value and actual need of coolness of mind and independence of sympathy on the part of the physician in the presence of his patient, mainly for the protection and welfare of the patient, whose life may rest in the maintenance of the undisturbed judgment of the practitioner, but in some degree as well for the self-preservation of the physician himself.

An equal period of intimate relation with students of medicine has made me realize well and comment more than once upon the similar need of mental coolness and collectedness, deliberation, and restraint on the part of undergraduates; just as my former teacher sought to inculcate an evenness of balance and imperturbability in his pupils passing into the active practice of their profession. And if, with such singular precedent and at a time when many of you are filled with ambition and emulation for a new field of action, I choose to refrain from the tedious disquisitions of the coming days and to speak at liberty of an attitude of mental preparation for your work and environments, I hope I may meet your sympathy.

I need only refer in passing to that almost obvious phase of the need of equanimity on the part of the student of medicine in his personal attitude to the individual diseases and symptoms as he is seeking familiarity with them. The development of this feature is too close to hand to require full comment. Those of you who have passed through the psychic pathogenesis of the list of human ills, from amebiasis to zymotic diseases, following in anguish system by system and symptom by symptom the lectures upon medicine and surgery, know too well the features one would rest upon, the illustrations one would offer, and the whole argument of dissuasion essential to the discussion of this all too common pathophobia which presents itself year in and year out as medical students pass onward in their studies. And I fear that, spite of all I might say, those of you who are for the first essaying your medical training will require personal experience to appreciate either the agony of imaginary disease, the importance of mental impressions upon the whole physical body, or the need of imperturbability lest our impressions of extrinsic disease react upon us. Impressionability is a real good, but not an unmixed possession. We are all too near the egoist not to be in danger of intro-application and of permitting our imaginations to predominate over our reason.

Those aspects of your work within these gates in which I feel that one might with truth and some force indicate the desirability for the student of holding himself in mental control and evenness of spirit embrace a rather wide series; but time and my own appreciation that they are largely matters for individual contemplation urge that on this occasion I limit myself to but two or three phases which spring directly from the student himself and certain reciprocal responsibilities which I believe rest upon the school authorities.

There are many persons so constituted that to them there can be little of attractiveness and interest in the contemplation of disease and in the studies which make up the medical curriculum. That there are such assemblages as this at this period of the year all over the land, that there are physicians who disregard personal pleasures, manifest a proverbial indifference for financial emolument, and who have developed as a second nature a carelessness for the common discomforts for the sake of their studies and practice, are sufficient evidence, however, that in reality the medical study and life have their own inherent attractions, pleasures and inducements; and to each of you, if you have entered this school aright, there are bound to be subjects laid before you which appeal particularly to your imaginations and sympathies, and probably, conversely, others for which you feel more or less indifference if not actual aversion. It is unlikely that in inception inclination will spontaneously incite to even application in all the branches upon the official schedule. In the first place, let me caution you that such unevenness in apparent disposition is not necessarily indicative of genius seeking its sphere, or of hopelessness for the eventual development of interest and success in those subjects which primarily do not appeal to you. There are those, it is true, who feel that such bents of mind are veritable indications, that they should not be interfered with, but should

at once be recognized and favored with the hope that special fitness be developed and possible genius stimulated; and it can scarcely be denied that occasionally the results justify such hope. But it should be kept in mind that in the end hard conditions and not mere theories are to be met, that the actualities of disease and death do not fit themselves to mere mental manipulations, and that only when genius can adapt itself to the natural lines of cleavage in the rock of the unknown is it permitted to penetrate beyond the depth which is open to us all. Genius may be wasted in medicine quite as much or more than in other fields of human thought —more, because in medicine and its cognate group the problems are so varied and so intricately conceal themselves. The very opposite is more frequently true in our profession than that genius asserts itself best when left from the start to follow its bias. The conditions which permit and the limitations which hamper accomplishment are too complexly arranged to allow more than in the veriest exception a straight line of pursuit, a single mode of attack for any question. Genius manifested by accomplishment represents but a minor fraction of potential genius, successful in spite of difficulties rather than because conditions and limitations were fitted for peculiar ability. Manifested genius in medicine is far more rare than in the mechanic arts, as the complexity of the living organism is beyond that of hand-made mechanisms; and stand out like Pasteur or Virchow, fixed upon breadth and sureness of preparation rather than evinced by mere penetrative acumen in a narrow scope. Each problem of life thus far solved has only opened to others equally elusive, and oftentimes ranging far from the direction of study leading to it; and clear interpretation usually demands far more than a limited basic information, but usually the accumulated knowledge of a number of workers approaching it from different lines of study. I say these things to you who are rich in hope and the future gifts of coming years. Success in medicine—not success in financial and popular returns; these depend on other factors and prove but little the possession of scientific ability or skill—success in medicine awaits in richest measure the greater number because of their breadth and accuracy of basic study, because of their fuller apprehension of principles rather than their possession of isolated facts, because of the preparedness of their evenly poised intelligencies and widely capable and educated minds. There is nothing in the fundamental portion of the medical curriculum from which I could in conscience excuse you or with which I could permit you dallying; and the brevity of human life and man's natural limits alone prevent my assertion of the necessity of the wider extension and fuller depth of your fundamental studies. I would insist with all the power I can give that you approach your profession in this spirit—that nothing is to be evaded, that here in your formative years you are preparing yourselves for the most diverse difficulties. There may be studies of no impelling interest to you, branches the application of which you do not with any clearness apprehend—one may not at first understand why for more than academic reason he who hopes to be a surgeon should be as faithful to the chemical or pathological laboratory as to the dissecting-room, or be as enthusiastically devoted to embryology as to bandaging. But because the correlation and application are not always at once clear, hold from declaring that they do not exist. Other men have passed by the same road you are travelling, and have said as I beg of you not to say. Some of them, it is true, have never seen reason to change their opinion, formed as it was in ignorance—but they have continued in ignorance and their loudly proclaimed declarations of the inutility of this or of that study you will find, if you search properly, are but loose cloaks covering a multitude of lost opportunities and mistakes, of which some were surely fatal. A man who has never seen can never appreciate color; and the man who lacks some knowledge fundamental to this or that phase of his practice can never know truly what he might have accomplished had he been possessed of it. The student who neglects his normal histology must either return to it or never appreciate the cellular structural faults which occur in disease, will consequently be sure to fail of comprehension of their faulty physiology, the development of symptoms, and the interrelations of the primary affections with the rest of the system. He may by compliment be said to practice medicine, but he cannot be said to know medicine.

Is there need for specification? You know how frequent is this tendency to evade tiresome work on the part of a large proportion of students, how with many, particular bug-bears arise, and how with individuals with or without apparent reason some particular subject assumes repulsive appearance. I appeal especially to those of the first and second years of our course of study, to students of the basic years, although in much it is equally applicable to the entire period of medical study. Your time for specialization has not yet arrived. You are here for the purpose of establishing your fund of basic principles; and as they are here acquired they are apt to follow to the end of your days. Be even in your judgment, and not swayed by whim or fancy, and adhere to a plan of equal and sane application in all lines which contribute to the foundation for your future work; and neglect not one thing of those which are offered lest some day the neglected information may mean loss of life for one of your patients or certainty of failure in some personal endeavor. If latitude is to be permitted students' choice let it be later, in the details of the applied branches, and certainly not in the basic and important technical parts of even these.

Approach your studies with a sense of charity for the faults

which human ignorance permits to remain in them, but with confident faith of their eventual dissipation and in the inherent harmony which must prevail. It is difficult, it is true, to realize such harmony and maintain the chain of thought where the links are faulty or missing; but one must know as well that certain parts of a theory are not proved as to know the proved portions in order to apprehend the value of the whole. The final proof of verity of any claim is the proof of the last-unsupported part. There are many such hiatuses in medical theories and your faith will often be demanded tentatively for an idea which "works out" in practice, even though its elements are not all established. Some of these very probably will eventually be recalled and others substituted for them; but meanwhile, with just appreciation of their weakness, accept such opinions as a basis for action, as "working theories," ready when the better appears to discard the insufficient. There are two groups of human beings from this standpoint and each is necessary to the discovery of eventual truth—those whose aim is constructive and whose imagination if uncurbed would quickly fill all gaps in our imperfect knowledge with what is best at hand, even though it be known to be imperfect—and those whose purpose is reductive, who seek out the imperfections that others have committed and lay bare by criticism the faults they may discover. Either of these, if extreme in type, is to be condemned, the one for foisting upon the fabrication material sure to be eventually dangerous, the other for tearing down without intention or expectation of repair the framework of the growing structure. If I may condemn the extreme I may, however, express sympathy for the less rash constructive theorist, who realizes the weak parts of his construction and while building seeks to correct them. I had rather approve the man whose ideas made him move out of his tracks as long as he tries to seek the proper direction, than one who refuses to budge because he fancies each direction wrong. All over the field of medicine you will find facts whose explanation is uncertain and weak; but if it be frankly acknowledged that the explanation is not perfect and must in the future be amended, I had always rather accept for the time the working theory (if it be not clearly untenable) than be without any conception. Your entire life in medicine, in practice as well as in your student days, will present daily opportunities for exercise of one or other of these inclinations; and if you are to be of most help hold a strict control over your mode of thought, refraining with earnestness from the extremes of either tendency, granting to both sane imagination and conservative criticism the good which each produces, and remembering that the ultimate end toward which you strive demands the exercise of each. Build symmetrically and advance, accepting for the time working material which if not quite perfect is at least not actually to be condemned; but keep your mind ever open to the correction which is eventually necessary for perfection.

The essentials of study are of course application and appreciation of each stage before a further step is taken. Every good medical school provides two means of preparation: one in principles, one in practice; and the former should always precede and lead into the latter. It was long since recognized that time, energy, and efficience are wasted by reversing this order. Schools of medicine would continue to share their students with private practising preceptors were this not true; and the habit of excluding first- and second-year students from the clinic-room and hospital ward is the outcome of recognition of this fact. You will find it a waste of time to take up even the text-books of the course without discrimination. The superficial familiarity in the clinical subjects which a beginner sometimes possesses is not a matter of important value and may be prejudicial by implanting the habit of uncertainty; and it is apt rather to be the pursuit of morbid curiosity than of sane energy which leads the first- and second-year man to devote any proportion of his time to contemplation of applied medicine—in which obstetrics and the venereal diseases are commonly the earliest thus investigated. The graded arrangement of studies in the curriculum is the result of deliberation on the part of experienced teachers; and it need demand no serious difficulty to apprehend the advantage of definite system in following the task of education. The nurse, training in the hospital wards, because of her constant presence with the sick, may and usually does acquire an enviable readiness of recognition of the surface features of disease; but beyond this point she does not advance, and year by year sees class after class of medical students, with less intimate acquaintance with the patient, but with clearer and more familiar understanding of the malady than her training afforded, advance to direct her ministrations. It will not be difficult for you in the future to pick from your medical acquaintances men whose adaptation is nearer that of the nurse than of the physician; and it will be rare that the student history of one of these does not tally with what I have been suggesting—the cart before the horse (and not improbably more cart than horse).

There are two recognized purposes of study which in very important measure influence method of study—study for information and study for power. It is unfair to insist upon their absolute distinction or to claim unreservedly either as the single characteristic of this or that school. But in a broad sense the first is perhaps seen in its higher dominance in our own schools as an inheritance from England, and the second in the schools of continental Europe. In enforced degree the first would have the student memorize the knowledge already acquired by his predecessors and accept the principles determined, familiarizing himself with a multi-

plicity of examples for the safer application of the inculcated facts; while in equally forced interpretation the second method would insist that the student devote his efforts to working out for himself a few concrete examples and aspire rather to farther penetration into the unknown than to burden his memory with the results of his father's experience. The average results of these two methods may be easily conceived to be—for the first, earlier efficience of the individual in the practical working of his profession within the scope set by his educational acquirements, but an inability to venture with confidence into untried fields or far beyond the limits he must acknowledge; for the second, a narrower scope of immediate readiness, the danger of rash attempt without experience, but the chance of ultimate, brilliant success beyond the hope of the ordinary. The history of American efficiency in the fields of operative work, based upon the pioneer studies of Pasteur and Lister, contrasted with the acknowledged dominance in scientific medical theorization and discovery by the Germans, with their equally acknowledged practical inferiority, illustrates in a broader way the trend set by these modes of education. It is not altogether a matter of choice between these methods with you; but there is a distinct field for deliberation and choice at your hands for some exercise of the latter, and there is ample reason to look forward to considerable extension of this privilege in American schools in the near future. Many of our institutions are now and practically all American schools of a generation ago were wedded to the first method, mills into which between rigid upper and nether stones the student was forced into the acquisition of a certain number of facts and gaining of a given degree of facility in the domain of the known—bettered in recent years in very material degree by laboratory exercises and personal student study of ward cases, but nevertheless not so unhampered as to permit enough concentrated effort for the student to gain his measure of power.

The value of human life and of the individual in America was greater in years past than it was in Europe or is at present among us; and the fear of sacrificing one life to unpreparedness demanded the immediate possession of a supposedly fair knowledge and facility in the details of practice by the candidate for medical employment. The general status of education in all branches and the ambitious zeal for quick acquirement and for independence of life kept this demanded modicum of training for years at a low level; and the medical class, in harmony upon the basis of inability to originate and fearful of testing others' views, followed far in the train of the world's progress. New things were viewed with doubt, and proof not sought independently, but demanded of others, before novel statements or methods were accepted. But the signs of the times are changing with us, have changed, indeed, and a mighty restlessness pervades the country in every direction, politically, financially, theologically, socially, and biologically. The popular idea of efficiency is attached not merely to the man who does routine things well, but also to him who does new things; and both from the incentive given by public opinion and from the advantages of increasing his usefulness we are bound to add more and more to the student's opportunity to gain personal power to obtain knowledge, in our fairly arranged organization for his assimilation of knowledge. Here in the pendulum swing of change lies no little danger, lest we forget our fathers too much and yield too much to the frenzy of restlessness which is abroad. The recent expansion of our country into imperial domain, the newer interpretations of our Constitution, the assumption of financial world-dominance, the promulgation of new and so-called higher criticism in religion, literature, science, and the arts, all mark our epoch as one of change. The marks of the same restlessness pervade medical schools and medical doings, a frenzy for action which in the main is beneficial, but which is full of signs of danger and futility; and there is need for sane and cool judgment as to how best to accomplish that which is best. That which has come last is by no means surely best. The new theories swing and sway in uneven circles about the old, now approaching and now receding from the teachings of former days, some assuming with time and familiarity the aspect of real widening of our ken, some drawn with their precursors back into the masses of wasted effort which lie in our fields of study side by side with certain knowledge. How far in this change is it profitable to urge the student to pursue his own way—what opportunities for independent work should be added to the existing scheme of American medical education? That such changes are certain to come in a greater degree than in the past is sure; the contrast between our own and European methods is too sharp and too widely and readily noted not to be accepted and eventually adjusted—although it may be promised that the assimilation of the procedures will not be limited only to one side. The good of each should be jealously preserved and the ultimate harmony obtained by mutual concession. For myself I feel that our rigid method of insistence should prevail completely throughout those parts of study which are fundamental and should include the essentials of system and technique of the applied branches and their special divisions. I feel that these might profitably be restricted to principles and to a much more limited exposition of examples and illustrations, depending upon the likelihood of only slow and minor changes in this scope. Such subjects as anatomy, general biological systematization, the principles of chemistry, and the major physiological phenomena, the procedures of obstetrics, the characteristics of proved pathogenical agents, their modes of operation and the typical results of their influence, the characteristics and modes of action of types of remedial agents and their methods of application, the well-

known manifestations of symptomatology and the approved methods of diagnosis, together with the technique of remedial operations, such studies as these, stripped of excess of repeated illustration, should be studied for information; and no latitude for evasion should be expected or offered in these from our scheme. In these subjects, mainly of the first and second year, but not entirely, economy of time and demand for future capacity demand the quickest and fullest acquisition; and such acquisition, it seems to me, is most surely gained by insistence upon class attendance, frequent examination by quiz or otherwise, consistent laboratory demonstration and exercise, and the perusal by the student of approved text-books and well-selected collateral reading. I would, with but occasional exceptions, advise the first- and second-year student against too wide journal reading; multiplicity of opinions and the conflict of investigation therein are more apt to be confusing than satisfying. But beyond the time when the fundamental knowledge is gained and a clear-cut picture of the field obtained I am ready to subscribe unequivocally to a plan of study for power for the individual; so that in the third and fourth years I warmly urge each man to take up along with the required class-work some one subject upon which he should read with fullest freedom that which is old and that which is new, that which is proved and that which is speculated, endeavoring to systematize for himself the material to a clear understanding of the existing aspect of the case, adding as far as he can active search for himself toward the solution of uncertainties or corroborating by repetition the accepted work of others. Such work I feel should be required in our developed scheme of education; and, subjected to proper inspection, should it show worth, should be credited to the student as a valuable substitute for his presence and attention upon the scheduled work which is purely illustrative or with facility obtained from text-books. I would not have it supposed that I am drawing back to the old theses of former years. The exhibition of theses in itself embodies the idea I would convey, provided the quality of the material justify; but if these writings be accepted when mere indiscriminate compilations they are quite insufficient.

The dissertations should be of the character and average worth of those required for gradation in German schools, each exhibiting the proved ability of the student in analysis of literature and in method of personal investigation. Were such theses presented as a voluntary effort I would at once advocate their consideration in the application for the doctorate; and could the scheme suggested be a definite part of the school-work I would grant an approved thesis the full dignity held by a major chair in the vote for the degree. Were it undone the degree should be postponed to its completion; were it a mere reiteration of text-book and encyclopedia articles it would be declined and the student required to produce something more worthy. For such work I would recognize the need of time and arrange for liberty from any but the periods of fundamental study and from all those subjects in which the student's investigations harmonized with the matter before the class. Herein lies, of course, a certain difficulty of arrangement, but I am confident it is not insuperable; and the added value of each man to himself and to the world would in such a scheme well justify his absence from lecture or ward during the time consumed.

This matter I feel lies before both student and faculty. Schools have as their primary purpose the instruction of men, but that instruction should comprehend both fixed knowledge and training to acquire. If there be acknowledged, as is so widely demanded, also the production of knowledge by the school as an essential function, I feel that unless it combines the expensive staff of investigators belonging to institutes of research with the usual staff of instruction of undergraduates, to overlook the potential advantages of an intelligent and interested student-body is a serious neglect of power. If it be declared that such divisions of time endanger the school's precedence in competitive and State examinations, I urge that the theses be offered definitely as part of the credentials sought by such examinations for fitness. It would be a rare man who would admire a meritorious, scientific production and refuse to credit its producer some advantage in an examination for capability and preparedness. The real aim of all education is that of acquiring preparedness, which lies in a great measure in the actual possession of knowledge, knowledge of fact, knowledge of reason, knowledge of method. Abstract knowledge is power, but not the only power; and the well-rounded man requires both the substratum of well-arranged and certain facts and the trained ability to add for himself to such a foundation. These suggestions I make are far from original; they are and have been for years the subject of earnest thought and attempt by many; here and there they are bearing fruit of promising worth in American schools; and they are sure to be pressed forward more and more as the new years elapse. The danger of overconfidence in the new methods demands that here we maintain a mental equilibrium; the danger of undervaluation I feel lies more with the students, and I urge your earnest thought along such lines—so that together we may arrive at the best result, maintaining the principle of rigidity in principles and of flexible adjustment of the secondary details to the need of acquirement of power.

Finally, in summation, I ask of the classes before me that you keep this attitude of mind, well knowing that, once assumed, it will continue with your life—that your purpose here is to acquire a broad, fundamental training in the essentials and that in no wise can you afford to neglect one single phase of it all; that you will devote yourself to it

with system and without either unbounded enthusiasm or with carping criticism, and that you hold in mind that an equal effort is deserved to gain the power of study as to acquire familiarity with facts.

I know I but voice the hearty sentiments of all my colleagues when, as I do, I welcome back the old student-body and hail the new, and ask of you all that you believe we regard it a privilege to be your friends, to be approached for whatever aid it is possible we can give you or for whatever advice may help you out of difficulty.

INJURY TO THE CONUS TERMINALIS (CONUS MEDULLARIS).[1]

By M. H. Fussell, M.D.,
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On account of the comparative rarity of lesions of the spinal cord confined to the extreme lower end, the following case is reported together with a few cases from the literature, some of which have much the same group of symptoms and which have come to autopsy.

Joseph Y., aged sixteen years. Parents both living and well. Is one of several healthy children. He was perfectly well until October 1, 1905, when he fell from a tree, striking on his back when reaching the ground.

The patient was first seen about half an hour after the accident. He was profoundly shocked. He was able to stand with difficulty and complained of much pain in the lumbar region. When lying on the ground he could move both legs equally well apparently with normal ease. There was a slight contusion over the first lumbar vertebra, but there was no pain on percussing the vertebræ.

He was sent to his home and visited the next morning. At this visit he had entirely recovered from the shock and could stand. He walked with some difficulty, however, the back held rigidly straight and the knees slightly bent.

He had retention of urine, the bladder causing a large tumor in the lower abdomen. The bladder was catheterized and it was observed that the urethra was insensitive. On further examination it was observed that there was no paralysis of the muscles of the legs. There was no toe-drop. The patellar reflexes were entirely absent even when reinforced and there was no plantar reflex. The next day the patient complained of some soreness over the lumbar spine. There was no prominence, however, and no pain on pressure. The same peculiar gait was noticed.

There was complete anesthesia of the penis, the scrotum, and a saddle-shaped area on the buttocks and posterior thigh, about as figured (Fig. 1). As is seen in the illustration, the area of anesthesia did not extend quite as far on the left thigh as on the right. The upper level, however, was about the same on both buttocks. There was complete paralysis of the anal sphincter and vesical sphincter. Urine was retained until the bladder became overdistended and then there was retention overflow. The anus, like the urethra, was insensitive. No rectal injection was of value. When a purgative was given there was complete incontinence of feces.

On October 15 the following note was made: Sensation over the previous anesthetic area is improved (unfortunately the sketch was lost); there is still paralysis of anal and vesical sphincters, though the bladder can be voluntarily emptied to a slight extent. There is still retention overflow, however.

On October 17 the patient is out of bed and walking with anesthesia about as before.

On October 21 there was an apparent slight prominence of the thoracic vertebræ in lower portion. The area of anesthesia is diminished. There is still incontinence of feces and urine. A plaster jacket was applied and gave relief.

On December 13 there is complete loss of patellar reflex. There is still some weakness on walking, especially on going up stairs. Still incontinence of feces and urine. There is no plantar reflex.

The area of anesthesia is much diminished and embraces about the fourth and fifth sacral areas on the right and the fourth and fifth on the left (Fig. 2).

One feature of the case, which was present in the beginning and which is most marked at present, is that there is slight swaying when he stands with his eyes closed. Patellar reflexes are still absent.

He walks, but the back is stiff and the knees bent. Drawing of a pin across the buttocks can be felt, while a pin prick cannot be felt. There was complete analgesia, anesthesia, and loss of heat sensation over the affected area.

At present examination there is slight paresis of leg muscles, but not so pronounced as in the beginning. He walks with rather a heavy step, as though he did not have control of the thigh muscles; wears off the heels of shoes in walking; cremasteric reflex is present on left; is developing a varicocele, possibly due to urinal which he has been wearing; scrotum still insensitive; testicle still insensitive; still has incontinence of urine and feces; no ankle clonus; muscle jerks of quadri-

[1] Read before the Philadelphia Neurological Society.

ceps slightly retained; Achilles reflex absent; plantar reflex absent; patellar reflex absent.

April 28, 1906. The area of anesthesia is the same. There is a trophic ulceration just at the fold between the buttocks; the ulcer is deep with raised edges; the toes of both feet are sharply flexed; the urine is foul; there is still incontinence of feces.

September 8, 1907. The patient was seen a few days since. He is in practically the same condition as at last note.

The points of interest in this case are:

1. The injury.

2. Very slight weakness of the legs, with continued and total loss of patellar reflex.

3. The incontinence of urine and feces.

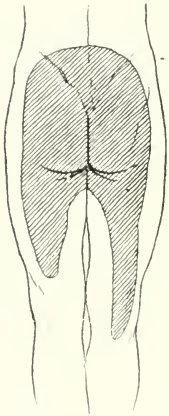

Fig. 1

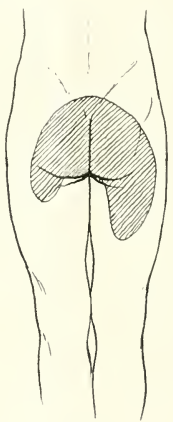

Fig. 2

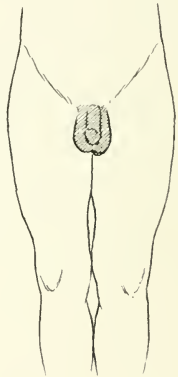

Fig. 3

4. The area of anesthesia comprising the saddle-shaped area supplied by the third, fourth, and fifth sacral nerves. The anesthesia of the external genitals and the urethra.

5. Catheterization became unnecessary after a few days.

Thorburn in his work on *Surgery of the Spinal Cord* quotes several cases which much resemble the one here reported.

Thorburn's cases are as follows (Huber, *Wiener medizinische Wochenschrift*, 1888, Nrs. 39 to 40): A man, aged twenty-four years, fell some six yards on to a paved street, alighting in a sitting position. He immediately felt great pain in both tubera ischiorum, in the lumbar region, over the sacrum, and along both sciatic nerves, and he could not stand. From the moment of the accident he had retention of urine, with involuntary evacuation of feces, accompanied by obstinate constipation. He could hardly move his legs, and had a feeling of numbness in them. The sacral and gluteal regions were very tender. After about a month he could stand and walk, and at that time he came under Huber's observation. He then complained of retention of urine, incontinence of feces, slight weakness of both lower limbs, and numbness in the soles of the feet. There was no paralysis of either limb, and the reflexes (superficial and deep) were all normal. He was found to have anesthesia about the anus and seat, in the perineum, scrotum, and penis, and on part of the posterior surface of the upper parts of the thighs. The boundaries of this region were not sharply defined, and will most readily be understood from the accompanying representation of Huber's diagram (Fig. 4). Although the scrotum was anesthesic, the testes were not. There was very dull sensation on passing the catheter or introducing the finger into and pressing upon the rectum. An ill-defined sensation was noticed before the feces were passed. The walk was normal and without pain. He could bend back, but on bending the knees had slight pain in the calves. There was no deformity of the back. Some three months after the accident it became unnecessary to use the catheter, as the patient could by strong pressure on the bladder cause the urine to flow slowly. He had sometimes partial erections of the penis, not, he thought, sufficient for copulation, and two or three times there was an escape of semen, with slight voluptuous sensation, there being no ejaculation, but only a slow escape from the urethra.

Huber's diagnosis is intrameningeal hemorrhage below the lumbar enlargement, which for a short time compressed

the cord itself, causing the paralysis, and is still pressing on the roots of the pubic and coccygeal nerves, as well as on the lower roots of the sciatic nerve, which furnish the small sciatic branch, the latter being affected less than the pubic and coccygeal. There was no evidence of fracture, and the immediate onset and other symptoms negative myelitis.

Bernhardt ("Injury in Lumbar Region, Involving the Third Sacral Roots," *Berliner klin. Wochenschrift*, August 6, 1888):

On January 10 a patient fell on his seat from the second floor of a building, and, not losing consciousness, complained only of pain in the back and retention of urine. On the following day he had to be catheterized, and he passed his feces involuntarily and unconsciously. Nine days later he could stand alone, but had pain from about the seventh

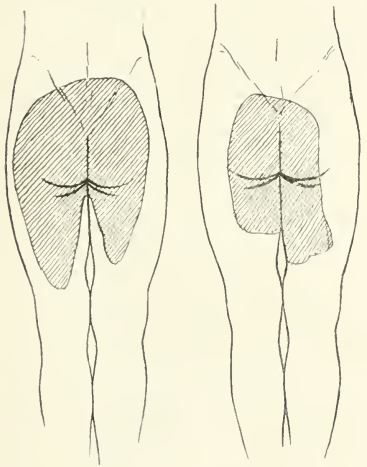

FIG. 4 FIG. 5

to the twelfth dorsal vertebra, where there was some swelling and tenderness. He had still retention of urine and unconscious defecation. There was no paralysis of the lower limbs, the superficial and deep reflexes were normal and, except in one region, sensation to all varieties of impression was normal.

Anesthesia was, however, complete in the perineum (but he could feel pressure on the testicles), penis, over the lower part of the sacrum and coccyx, and thence outward for about a hand's breadth, as well as down a strip on the inner and posterior aspect of the thighs, indicated in the accompanying illustration (Fig. 5).

The patient continued to use the catheter, but had no sensation of the bladder being full. He could feel by abdominal movements when he passed feces, but did not feel their course through the rectum or anus. He sometimes had erections, and once a pollution, and in February he performed coitus. By May he sometimes could pass a little urine, but never completely emptied the bladder, and if he was not catheterized the latter would ultimately become overfull and urine would flow.

Oppenheim ("Fracture of First Vertebra; Crush of Cord About Level of Origin of Third Sacral Roots," *Archiv f. Psychiatrie*):

A man, aged twenty-four years, fell from the second floor of a house, alighting on his sacrum. After a brief period of unconsciousness he noticed numbness and paralysis of both lower limbs, both of which symptoms rapidly passed away.

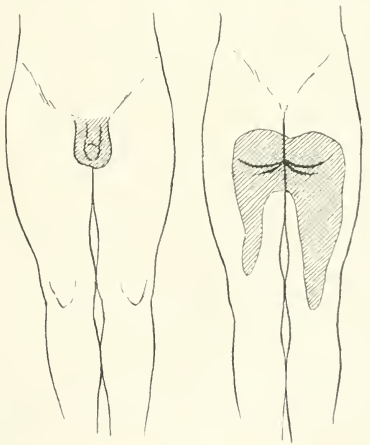

FIG. 6

He had immediate retention, followed by complete incontinence of urine and feces, with unconsciousness of their passage. Neither erections nor passage of semen ever occurred after the injury. At the region of the first and second lumbar spinous processes was some angular curvature. Of the muscle of the lower limbs those of the calf only showed very slight weakness; otherwise there was no loss of power and no atrophy or electrical change. The knee-jerk was exaggerated, but there was no ankle clonus. Anesthesia affected the region of the anus, buttocks, perineum, scrotum, and penis, and a small strip on the inner and posterior aspect of the upper part of the thighs above; it was limited by a line about half-way down the sacrum, and externally it extended to midway between the tuber ischii and greater trochanter.

Cystitis and fever supervened, the patient dying about three months and a half after the injury.

At the postmortem examination a fracture of the lumbar vertebra was found. The terminal portion of the conus medullaris was compressed, showing the histological appearances of myelitis with hemorrhages, and the lowest sacral roots were degenerated. The remaining roots of the cauda equina were almost absolutely normal.

Osler ("Injury in Lumbar Region Involving Third Sacral Roots," *Medical News*, December 15, 1888):

A man, aged forty-seven years, fell from a bridge into a sitting posture, and at first sustained paralysis of the legs, bladder, and rectum, the paralysis of the lower limbs passing off gradually. Sixteen years after the injury he had slight weakness and atrophy of the lower limbs. The spine presented no local signs of injury. He had no control over the bladder and rectum, and was impotent. The gluteal and cremasteric reflexes and the knee-jerk remained. Anesthesia is represented in the annexed copies of Osler's aspects of the thighs, perineum, and penis as far as its root. The urethra was also insensitive (Fig. 6).

Muller (*Deutsche Zeitschrift f. Nervenheilkunden*, vol. xiv) shows diagrams agreeing entirely with the diagrams here exhibited. In the course of his masterly and exhaustive article he says:

"The nerves of the cauda equina are not peripheral nerves, but must be considered as part of the cord bundles, as there are motor and sensory fibers.

"It is of the utmost importance to note that the anterior and lateral portion of the pelvis and the upper part of the thigh derive their sensory fibers from the lumbar plexus, while the penis and the scrotum receive their sensory fibers from the sacral plexus. The testicles themselves, however, are supplied through the external spermatic from the upper part of the lumbar plexus. So it occurs that in paralysis in the region supplied by the sacral cord at sacral plexus, pressure on the testicle gives no sensation from the scrotum itself, but the testicle recognizes the pressure."

He quotes several clinical cases. First case, the second, third, fourth, and fifth sacral segments are involved, and this case has the same condition concerning reflexes as the one here reported, *i. e.*, the cremaster reflex and the abdominal reflex are present, while the patellar, Achilles, and plantar reflexes are entirely absent.

Osler, in the last edition of *Practice of Medicine*, says:

"A lesion limited to the conus medullaris is rare. A myelitis or a focal hematomyelitis may be limited to this site, with symptoms referable to a lesion of the lowest sacral segments; anesthesia over the buttocks, perineum, and genitalia; paralysis of the levator ani and the vesical and anal sphincters.

"Such a localized lesion has been known to follow a lumbar puncture made between the first and second lumbar vertebræ.

"In a fracture or dislocation of the first lumbar vertebra the conus medullaris may be compressed together with the lowest sacral nerves given off from it. It is rare, however, in traumatic cases for a tip of the cord to suffer injury alone without simultaneous involvement of the nerve roots comprising the cauda equina from the second lumbar down.

"It would then appear that this lad has received an injury involving the conus medullaris at the third, fourth, and fifth sacral roots."

According to Osler's diagram the second sacral is also probably involved, but, as quoted above in the cases with autopsies, the lesions appear to be below the second, but involving the third nerve.

The case differs from these here quoted and from one reported by Weisenberg in that the patellar reflexes are absent, while in the other cases the patellar reflexes were either exaggerated or normal.

The age of the patient precludes the possibility of knowledge as to the effect of the injury on the sexual functions.

TENDON TRANSPLANTATION.[1]

By John H. Jopson, M.D.,

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The operation of tendon transplantation may now be said, without dispute, to be one of the most valuable procedures in the treatment of certain types of paralysis and deformity. Attracting little attention at the time of its birth, allowed to slumber in obscurity for a long time, it was finally seized upon with avidity and pressed into service in the treatment of a respectably long and sufficiently varied list of deformities. Nor has it escaped the usual fate of new discoveries. Made the subject of extravagant claims, it was inevitable that it should later pass through a stage of harsh criticism and condemnation from those disappointed by their failure to achieve the impossible. It has, however, survived this most critical period of its existence, and from the literature now appearing, one may gather, the almost universally favorable verdicts as to its usefulness. Moreover, the study of the technique of

[1] Read before the Surgical Section Pennsylvania State Medical Society, Reading, September 26, 1907.

the operation has been pursued and a wealth of experimental and clinical observation has been and is being analyzed, with a view of improvement of operative results. Indeed, we find the types of operation practised today widely differing from the procedure originally undertaken by Nicoladoni.

The Types of Deformity and Paralysis Suitable for the Operation. To what conditions is the operation of tendon transplantation suitable? First in the list stands *infantile paralysis*, as offering its greatest field. When we appreciate the object of tendon transplantation, the shifting of the point of action of a healthy muscle from its original insertion, where its action is superfluous or deforming, to another point, so as to replace that of a muscle or group of muscles whose activity has been diminished, its applicability to infantile paralysis is apparent. We have to do here with a disease that wipes out the cells upon which certain muscles are dependent for innervation and, with its irregular action, often leaves in anatomical relationship, and in a situation operatively accessible, other muscles in a normal state of health or with only temporarily impaired activity. What more natural than to substitute in toto the activity of the one for the other, even though a change of function may be necessary, or to divide the power of the healthy muscle between two points of insertion? It is, therefore, in infantile paralysis, whose irregularity of muscular distribution is sometimes a blessing in disguise, that tendon transplantation finds applicability to the greatest number of cases.

Cerebral spastic palsy, while a less promising field, offers certain indications and opportunities for tendon transplantation that are winning a belated recognition. The combination of paralysis and spasm in these cases, to say nothing of the frequent association of mental deficiency, makes the devising of a plan of operation more difficult. The recent work of Vulpius,[1] Tubby,[2] Jones,[3] and Perl[4] offers encouragement to future development in this line. It has been shown that not only can deformity be lessened or corrected, but that function can be increased, thereby fulfilling both the indications for its use that are frequently laid down. Moreover, there is effected a lessening of the spasm after tenotomy and tendon transplantation, which often proves to be permanent. While in infantile paralysis the lower extremity offers the greatest opportunity for operation, the upper extremity, especially the forearm and hand, is frequently susceptible of improvement in spastic palsies. As types of operation may be mentioned Tubby's and Hoffa's operations upon the pronator radii teres. Both convert it into a supinator: one, by changing the insertion of its tendon; the other, by altering its point of origin.

In *congenital club-foot*, tendon transplantation has been recently recommended and practised with benefit (Ashhurst).[5] That it is indicated in more than a small proportion of cases is doubtful. Deformity must, in any case, be thoroughly overcome by other means as a primary measure; and if the foot can be maintained in a corrected or overcorrected position until the rudimentary or congenitally weakened muscles have an opportunity to develop, there would seem to be no good reason for shifting tendons. In a certain number of cases, however, it has been found of advantage; and its field of usefulness may, in time, be much enlarged.

Its application to *traumatic and inflammatory types of deformity* is limited by the smaller number of suitable cases. It is, however, in such cases that it will be found of greatest value to the general surgeon. When muscles or tendons are destroyed by accident or disease, he can, therefore, sometimes practice transplantation with benefit.

Birth palsies, especially those affecting the shoulder group, are susceptible of operative treatment, aside from the recently proposed treatment by nerve anastomosis and resection, if there remain healthy muscles, in the shape of the trapezius or pectoral, to replace the deltoid and biceps.

Finally may be included *progressive muscular atrophy*, a condition whose very name would seem to forbid attempts at relief by surgical interference. Both Hoffa[6] and Vulpius,[1] however, have pointed to a ray of hope for improvement in this otherwise almost hopeless condition. Both these authorities have testified to the improvement to be obtained in a certain few carefully selected cases, in which an arrest of the progress of the disease for a year or more offers the opportunity to make the patient more comfortable and self-helpful during such a period. It must be understood that such relief is but temporary; and Oppenheim's objection, although it seems to us well contradicted by Hoffa, may yet prove valid, and remove even the corporal's guard of cases from the eligible list. The results, however, are good enough to warrant further observation. While this list does not include all the conditions in which tendon transplantation is indicated, it will suffice to indicate most of the types of paralysis and deformity to which it has been applied.

Selection of Cases. Something more than the diagnosis is necessary as a preliminary to the carrying out of the operation. The selection of appropriate cases, their careful study, and the execution of certain preliminary steps are essential before proceeding to the operation itself. Many of the early failures were due to an improper selection of cases. Cases of total paralysis are entirely unsuited to this operation. Where no power remains to be applied, no especial benefit can be expected from transplantation. Any benefit that can be obtained can be duplicated and better accomplished by tendon shortening and arthrodesis, as the transplanted tendons act only as additional ligaments. In cases of paralysis less severe, but still extensive, benefit can sometimes be obtained. Of these it must be said that cases admitting of simplicity of operation give more satisfactory results than do

cases in which multiple transplantation and complicated schemes of operation are necessitated.

In infantile paralysis, a sufficient length of time must have elapsed since the onset of the paralysis to permit of the fullest restoration of power that can be hoped for by nature, assisted by massage, electricity, and a full correction of deformity when present. This point has been so frequently emphasized that it is merely necessary to repeat that one year—or, better, two years—should elapse before transplantation is attempted.

The necessity for preliminary correction is probably not yet sufficiently appreciated. By preliminary correction of contractures, by manipulation and tenotomy, followed by the application of a mechanical appliance, the overstretched and paretic muscles frequently regain a certain amount of contractility and tension. Tendon shortening has been observed to have a similar beneficial action on apparently paralyzed muscles. The results of transplantation will, then, be better when the time comes to put it into practice.

A careful preliminary study of the case is, of course, essential. The muscles must be studied, not only in connection with their electrical excitability (an uncertain test), but by palpation and a study of their voluntary uses in movement—walking, etc. The influence of healthy muscles on deformity and their relative importance in the primary movements of the foot must be investigated.

If doubt remains as to the exact state of health of individual muscles, a certain latitude in the plan of operation may be allowed until operation is undertaken, when an extension of the incision will enable one to examine them and to distinguish between the dark-red color of the healthy muscle, the lighter tint of the partially paralyzed muscle, and the yellow hue and atrophied state of the muscle that is the seat of advanced degeneration, its tendon no longer glistening, but of a dull, yellowish white.

The relative importance of the primary movements of the part must, as Whitman[7] points out, be borne in mind. In the foot, these include plantar flexion, dorsal flexion, adduction, and abduction, mentioned in the order of their relative importance; and all are of more importance than the power of movement in the toes. In the forearm and hand, the movements of the fingers are of much greater importance than are the movements of the wrist. It is of great importance to restore the most useful, and not to weaken a more useful for a less useful function. Again, the relative strength of the transplanted muscle must be borne in mind; we must not "send a boy to do a man's errand." Such transference may secure one object, to prevent relapse of deformity, but it cannot restore in full the function. When the transplanted muscle is a deforming agent, it may often be used to greatest advantage by shifting it where its action is exerted in the direction of correction. It is, moreover, advantageous to employ muscles whose new function is not antagonistic to others of the same group that are not disturbed. It is sometimes better, when necessary to alter the function of a muscle, to transplant the entire group of which it is a member, as in the case of the hamstring muscles (Lange).[8] The early and late results will be thereby improved.

In regard to the question of *splitting of tendons and muscles*, and transplantation of a portion only, this procedure of Drobnick's is frequently practised to advantage, especially in the gastrocnemius muscle. Seldom, however, does the transplanted portion of muscle develop independent action, except in the case of the tibialis anticus. The studies of Wollenberg[9] are of prime importance in this connection. In a study of the course of intramuscular nerve paths and their relation to tendon transplantation, he divides the results of this partial tendon and muscle transplantation into three groups: (1) Where independent muscular action is obtained in the transplanted portion; (2) where it acts simultaneously with the main body of the muscle; (3) where it loses entirely any contracting power. Of these, the second group includes the greatest number of results.

Wollenberg's experimental studies showed that the nerves probably follow the arteries in their distribution, that this is commonly in the direction of a circular anastomosis from a central point, and that in only a few muscles, such as the sural and gracilis, is their direction a longitudinal one. It will be easily seen that the effects of splitting the muscle in most cases will be to divide many of the nerve fibers, and that the anatomical arrangement renders unlikely the development of independent action in the portion detached, to say nothing of the danger of atrophy, if the section be carried too far; although such atrophy, as Hoffa says, "Gott sei Dank recht selten eintritt." The portion split off, however, must not be too small; and the split must not extend higher than the middle of the belly of the muscle.

Muscle Transplantation. In some cases, the origin of muscles can be altered in such a manner as to bring about a beneficial change of function. Hoffa's operation on the pronator radii teres has already been mentioned. As a more radical measure, we may refer to the procedure of Hildebrand, as practised by him and by Sachs,[10] who, dissatisfied with transplantation of the trapezius into the deltoid, in paralysis of that muscle, have successfully substituted the pectoralis major as an abductor, by detaching it from its origin on the ribs, sternum, and clavicle, turning it at an angle of 90 degrees, carefully preserving its nerve supply, and attaching it to the spine of the scapula, the acromion, and the outer end of the clavicle.

Operative Technique. Many surgeons advocate the use of the Esmarch bandage. It seems to us that this favors consecutive oozing and makes temporary drainage necessary, where it might otherwise be dispensed with. The favorite suture material is silk. Chromicized catgut has yielded

good results in our hands, and can be prepared to resist absorption for a sufficient time in the average case. Silk is, however, necessary when Lange's method of tendon elongation is practised; and a finer suture can be used, and a smaller knot employed. The danger of secondary abscess formation from its presence can be avoided by rendering it antiseptic through boiling in, or prolonged immersion in, bichloride of mercury solution and dipping in melted paraffin before using.

Lange's method of *periosteal implantation*, in place of union to a paralyzed tendon, continues to grow in favor. Dane and Townsend's observations on the disappointing results of tendon to tendon transplantation are frequently quoted as evidence of the failure of the old operation (Taylor[11]). In spite of these objections, the old method still is oftentimes most feasible, and very satisfactory. The bone may be drilled and the tendon passed through the opening, as recommended by Müller. Chlumsky's[12] method of splitting the tendon, passing one-half of it through a drill opening and attaching it to the other half by mattress sutures is an elaboration of Müller's method. Silver's[13] valuable experiments show that we need not fear necrosis from tying our sutures too firmly; and also that many failures have been due to an insufficient hold or insufficient strength of the sutures. Lange's method of forming artificial tendons from silk sutures continues popular with many surgeons. Whatever method of transplantation is practised, a sufficient amount of tension in the transplanted muscle must be obtained, if satisfactory muscular action is to be hoped for.

Finally, it is now agreed on all sides that the after-treatment must be carefully and thoroughly carried out for a long time. Absolute fixation and rest for the primary period of repair, when the ensheathing callus is being formed, must be insisted on; and fixation by plaster must be maintained for at least six weeks. After the removal of the cast, the transplanted muscles should be protected from overstrain by mechanical means. The use of electricity and massage, and the education of the muscles in their new functions are imperatively demanded as contributing factors in maintaining correction and aiding functional development. Although the ideal result sought for is the dispensing with braces, we must not be in too great a hurry to bring this about, lest we undo the benefit gained.

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ARTERIOSCLEROSIS OF THE CENTRAL NERVOUS SYSTEM, WITH A REPORT OF THREE CASES.

By Henry S. Hutchinson, M.D.[1]

(From the Department of Neurology and the Laboratory of Neuropathology of the University of Pennsylvania, and from the Philadelphia General Hospital.)

Case I.—Devenny; spastic paraplegia; admitted January 24, 1906, in semistuporous condition, to the service of Dr. Spiller.

Physical Examination. An aged woman, sparse white hair; chest apparently clear, even hyperresonant to percussion. No heart murmurs. Arteries markedly sclerosed; pulse feeble; abdomen board-like.

Extremities. The arms are flexed at elbows and crossed over the chest; muscles are spastic; the arms can be straightened when some force is used. Legs: Thighs flexed on abdomen and legs on thighs, especially the left leg, which lies directly for eight inches below the knee upon the thigh. On account of the spasticity, the reflexes cannot be obtained.

Only complaint is of being cold. Does not like to be disturbed for meals or for medicine.

February 1, 1906. Notes by Dr. Weisenburg: Patient's mentality is poor. Says she is worried because she does not feel well; she has no pain anywhere; seems to have bilateral cataract. Biceps and triceps reflexes are present and prompt. Has incontinence of urine and feces; no Babinski; sensation apparently normal.

Notes by Dr. Spiller: Both upper and lower limbs are markedly contracted in flexion and wasted, as is the whole body. The upper limbs can be forcibly extended at all parts, including fingers, but the limbs are very stiff. Mentally the patient is so feeble that no history can be obtained. Biceps tendon reflex is very prompt on each side. Lower limbs cannot

[1] Dr. Hutchinson was engaged in preparing this paper in the Laboratory of Neuropathology during his fourth year as a medical student at the University of Pennsylvania, and completed it shortly before his death. It is published as written by him.—William G. Spiller, M.D.

be forcibly extended as the contractures are so great. It is impossible to determine whether patellar tendon reflexes and Achilles jerks are exaggerated or not, because of the rigidity of the lower limbs. Pricking feet with pin causes pain. Diagnosis: Senile changes of the central nervous system.

February 17, 1906. Patient is in a stuporous condition. Hands and feet and face are cold. Pulse rapid and weak. There has been no bowel movement, in spite of enemata and medicine. Died February 18, 1906.

Microscopic examination of cord and brain showed the following:

Lumbar Region. There are distinct degenerative changes in the nerve cells of the anterior horns, these changes consisting in a breaking up of the chromophilic elements in the centre of the cells, with occasionally peripherally placed nuclei. The cells are heavily pigmented. The small vessels, especially in the posterior columns, show greatly thickened walls; and numerous bands of neuroglia are found within the cord substance, so that there is a considerable degree of diffuse sclerosis. There is no distinct degeneration of nerve fibers, either in the cord itself or in the anterior and posterior roots.

Thoracic Region. The thickening of the small blood-vessels within the cord is more pronounced here than in the lumbar region, and the sections are like those of certain cases of paralysis agitans. Sections stained by the Mallory connective-tissue method demonstrate these thickened and multiplied bloodvessels very well; and this stain also colors the amyloid bodies, which are seen in very large numbers, especially at the periphery of the cord.

Cervical Region. The cells of the anterior horns are altered in the same way as those of the lumbar region. Sections stained by the Marchi method, both of the lumbar and cervical region, show only a few scattered black dots, which are not indicative of degeneration.

Medulla oblongata shows nothing abnormal beyond the presence of numerous amyloid bodies.

Paracentral Lobules. The cells of Betz in both paracentral lobules show some alteration, consisting in central chromatolysis, displacement of the nucleus, and intense pigmentation. Even the small cells of the cortex are deeply pigmented. The small vessels are also much thickened. Amyloid bodies are exceedingly numerous at the periphery of the cortex.

Optic Chiasm and Optic Nerves. No degenerations are present in the optic nerves. The septa of the chiasm are greatly thickened, as are also the walls of the bloodvessels; and in the optic nerves a marked increase in neuroglia tissue is present. At the sides of the chiasm, numerous amyloid bodies are seen.

Olfactory Tracts and Bulbs. Along the course of the olfactory tract amyloid bodies in enormous number are seen, scattered between the fibers, and diminishing in number as the olfactory bulb is reached. The Mallory connective-tissue stain colors these bodies a deep blue.

Case II. Johnson, an old woman, unable to talk, was admitted to the Philadelphia General Hospital, service of Dr. Spiller, August 25, 1905. Notes by Dr. Weisenburg: Voice weak, uncertain; speech understood with difficulty. Pupils larger than normal, irregular; react slightly to light. Looks up and down easily, but only with difficulty to either side; can by a great effort perform associated movements. Reaction to light if present at all is very slight. Winks the right eye less often than the left, and when she winks both, the right lid is not closed tightly. Mouth drawn to the right; the right side of the face droops; puffing of the right cheek; tongue protruded to right side; has to be fed; is apparently completely blind; elevates the brow equally on both sides. Right arm and leg are paretic; some spasticity is present, but no contractures; reflexes on this side are prompt. Sensation to pain and touch, apparently normal all over body. Patient very emaciated; Babinski reflex not obtainable. Patient able to move right lower limb better than right upper limb. Each crystalline lens discovered to be cataractous. Chest: Protrusion of sternum. Fine moist rales heard over both lungs. Heart sounds faint and irregular. Slight diastolic murmur in mitral area. Pulse weak, irregular, and of small volume. Arteries greatly sclerosed.

At the autopsy the anatomical diagnosis was: General arteriosclerosis; chronic endocarditis; perisplenitis; chronic interstitial splenitis; chronic interstitial nephritis; cystic kidney; atrophic cirrhosis and passive congestion of the liver; thrombosis in thoracic aorta; hydrops of the bladder.

Microscopic study of the spinal cord and brain showed the following:

Lumbar Region. The cells of the anterior horns show considerable change, of the same character as in the previous case. There is occasionally a peripherally placed nucleus, and here and there breaking up of chromophilic elements. The cellular pigmentation is excessive, at times nearly the whole of the cell being taken up by the pigment. The bloodvessels, especially those in the posterior columns, show thickening. No distinct degeneration of nerve fibers in any of the tracts of the white matter. Not even in the crossed pyramidal tracts.

Thoracic Region. Appearance similar in every way to that in Case I.

Cervical Region. Changes in anterior horn cells same as those in the lumbar region. The thickening of the bloodvessels is not as marked as in the thoracic region. In the posterior columns, especially in their posterior portions, there is an evident sclerosis, the tissue here staining poorly by the Weigert hematoxylin. The sclerosis of the bloodvessels is not as marked as in the thoracic region.

Paracentral Lobules. Most of the cells of Betz are diseased; eccentric nuclei are seen, and many of the cells are diffusely stained and spherical in outline. Pigmentation is not as marked as in Case I. Thickening of the blood-vessels is very evident, both in the pia and within the brain tissue; and beneath the surface amyloid bodies are fairly numerous.

Optic Chiasm and Optic Nerves. Transverse sections of the optic nerves unfortunately were not cut; in the sections through the optic chiasm cutting the optic nerves longitudinally, the latter, besides showing great thickening of their bloodvessels, show many degenerated nerve fibers. Large numbers of amyloid bodies are present in the optic nerves.

Olfactory tract and bulb show amyloid bodies as in Case I.

Case III.—Bagnall, a woman, aged sixty-two years; occupation, housework. Admitted to the Philadelphia General Hospital, service of Dr. Spiller, March 3, 1906. Patient is weak and somewhat confused. Cannot answer questions intelligently.

History. Two years ago, two strokes of apoplexy. Two weeks ago, caught cold. Very debilitated, weak, and confused. Cannot answer questions intelligently. Old and wrinkled. Gait unsteady. Dr. Weisenburg's notes on her condition: Patient says she is thirty-six; obeys commands. Wrinkles brows equally well on both sides. On shutting eyes, power is apparently equal on both sides. On opening mouth and showing teeth, a weakness of the lower part of the right side of the face is apparent. The tongue is protruded to the right. The power in the patient's hands is diminished, equally so on either side. It is impossible to tell whether or not there is an old paresis on the right side. Biceps and triceps jerks cannot be obtained because the patient holds the arm so rigidly. Patellar and Achilles jerks are prompt on the left side; on the right side they cannot be obtained, as the patient holds her limb so rigidly. Eyes show arcus senilis; pupils normal in size but slightly irregular in outline. React sluggishly if at all to light and accommodation. Extra ocular movements performed fairly well. Tongue moist, broad, protruded in median line. No irregularities in facial lines; chest emphysematous; kyphosis is present in upper thoracic region. Expansion is slight; percussion gives slightly hyperresonant note. Crepitant and subcrepitant rales at the bases. Heart sounds fairly clear. Lower limbs show nothing abnormal,; knee-jerks and sensation normal. There is an area of inflammation over the right elbow. Biceps and triceps reflexes normal. Gait very unsteady.

March 30th. Patient's condition is getting much worse. She is very dyspneic, and her chest is full of rales. Heart rapid and weak.

March 31st. Urine: trace of albumin; few coarsely granular casts. Died today.

Autopsy. Anatomical diagnosis; congestion and edema of pia mater; brown atrophy of heart; chronic endocarditis; general arteriosclerosis; esophageal piles; enteroptosis; nutmeg liver; cyanotic induration of spleen; fatty, sclerotic pancreas.

Microscopic study of spinal cord and brain showed the following:

Lumbar Region. There is marked pigmentation in the cells of the anterior horns. The bloodvessels within the cord are thickened. By the Weigert hematoxylin stain the right crossed pyramidal tract is found to be slightly degenerated.

Thoracic Region. A very slight degeneration of the crossed pyramidal tract of the right side is seen. There is a very evident hydromyelia, the dilated central canal extending from the base of one posterior horn across the cord to the base of the other posterior horn. The cavity is lined by ependymal epithelium at certain regions, which seems to be undergoing proliferation and to be extending into the surrounding tissue. The bloodvessels in the gray matter appear congested. Amyloid bodies are present in large number, and the vessels are thickened.

Cervical Region. Most of the cells of the anterior horns are deeply pigmented, and some are entirely filled with pigment. Strands of tissue extending into the cord from the pia, and the walls of the bloodvessels are thicker than normal. There is slight degeneration in the right crossed pyramidal tract. The central canal is a little dilated. By osmic acid staining, some black fibers are seen in each crossed pyramidal tract, more numerous on the left side.

Medulla. More black fibers in right pyramid than in left.

Paracentral Lobules. The cells of Betz in each paracentral lobule are excessively pigmented. The bloodvessels in the pia and in the cortical gray matter are considerably thickened. Amyloid bodies are present, but not in very large number.

Optic Chiasm and Optic Nerves. No degenerations are found in the optic nerves; but each nerve shows a great increase in fibrous tissue. Amyloid bodies are present, especially, as in the other two cases, at the sides of the chiasm.

Olfactory Tracts and Bulbs. Amyloid bodies as in the other two cases.

A small area of softening was discovered in the lenticular nucleus of the one side. Examined microscopically, the tissue here is seen to be very much ossified.

Resume. The pathological findings in the three cases were fairly uniform. The bloodvessels throughout cord and brain were found thickened and at times with lumen obliterated, this condition being especially marked, in all three cases, in the thoracic segments of the cord.

The connective tissue in the pia was seen to be increased; that between the fibers of the optic nerves was markedly proliferated.

In the nerve cells of the anterior horns and in the cells of Betz in the paracentral lobules there was seen a variety of changes. In Cases I and II, both in the lumbar and in the cervical regions, the cells showed, in addition to intense pigmentation, distinct degenerative changes. Case III showed, in the anterior horn cells, merely an intense degree of pigmentation. The cells of Betz in the first two cases presented the same diseased condition as was seen in the anterior horn cells; in the third case, however, the cells of Betz were, aside from intense pigmentation, unchanged.

Quite remarkable were the enormous numbers of amyloid bodies present in the three cases. These bodies were seen all through the cord, at its periphery, beneath the pia in the cortex of the brain, at the sides of the optic chiasm, and in the olfactory tracts and bulbs.

As for nerve-fiber degenerations, none were present in either of the first two cases. Case III showed, by the Weigert stain, a slight degeneration of the right crossed pyramidal tract throughout the cord; sections stained by osmic acid showed a recent degeneration of the left pyramidal tract.

These cases, though offering nothing distinctly new either in symptomatology or in pathological anatomy, may yet serve as contributions illustrating the various manifestations to which arteriosclerosis may give rise.

The symptoms present in these cases are to be in large part attributed to the pathological changes found in the spinal cord and in the brain. Besides the evidences, both in cord and brain, of the poor nutrition which must have been consequent upon the presence of thickened and sometimes obliterated arterioles, there were, in the first two cases at least, distinct degenerative changes in the cells of the anterior horns and of the motor cortex. These changes, together with the intense degree of pigmentation seen in the cells, both of which changes were in all probability due to the cutting down of the blood supply, must be held to account for the paraplegia and the contractures in the lower limbs.

Arteriosclerosis has been much studied of late, especially that form of disease confined to the nervous system; and it has come to be recognized that an absence of thickening of the peripheral arteries does not by any means exclude the possibility of the presence, even in a markedly advanced degree, of sclerosis of the arteries of some internal organ. Within the last year a new manifestation of arteriosclerosis of the central nervous system has been described—that known as intermittent claudication of central origin. This disorder, first described by Dejerine,[1] in April, 1906, and later by Grasset,[2] Sollier,[3] and others, differs from the form of intermittent claudication dependent upon peripheral arteriosclerosis—a condition first recognized by Charcot in 1888—in several particulars; the signs of peripheral arteriosclerosis are absent (cyanosis of the part, coldness, loss of pulsation in dorsalis pedis artery); the knee-jerks, which may be normal or even decreased when the patient is at rest, become markedly exaggerated after exercise; the Babinski reflex may be present after exercise; there are generally bladder and rectal disturbances, and perhaps disturbances in sexual function.

In Dejerine's cases the symptoms came on only after exercise; after the patients had walked for varying distances there developed in the lower limbs first a sensation of heaviness, then an actual paralysis. After resting for a while, no muscular weakness whatever could be discovered, and the exaggerated knee-jerks and Babinski's sign which had been present disappeared. Since the peripheral arteries in the lower limbs were comparatively normal, Dejerine attributes the symptoms to an ischemia of the spinal cord, the result of an endarteritis.

Sollier[3] believes that the nature of the process is always syphilitic, in spite of the fact that many of those affected denied having had syphilis. An endarteritic process, he says, brings about an insufficient blood supply to the dorso-lumbar region of the cord, and so produces the symptoms.

Erb also emphasizes the distinction between the central and peripheral forms of arteriosclerotic lameness, and reports a typical case of the central type with relatively normal peripheral arteries.

Besides this form, various other symptom complexes, the result of arteriosclerosis of the nervous system, are reported in the literature. Thus, Collins gives an instance in which the symptoms came on so rapidly that the case was looked upon as one of Landry's paralysis. Buzzard and Barnes[4] report a case of a woman of fifty-three years, who had suffered for ten years with a gradually progressing weakness in the legs and the facial muscles; also from uncontrollable laughter. At autopsy, degeneration of the pyramidal tracts was found, which the authors attributed to the manifest disease of the arterioles. The cases reported by Pic and Bonnamour[5] showed a course characterized by "paretospasmodic" symptoms, exaggeration of reflexes, presence of the Babinski reflex, epileptoid trepidation, and weakening of intellect.

Hirsch[6] found, in a number of cases of "arteriosclerosis of the spinal cord," besides thickening and partial obliteration of the lumina of the arterioles, pathological changes in the anterior horn cells, and also minute hemorrhages into the gray matter of the cord. Such hemorrhages are also described by Warrington and Owen,[7] and are believed by them to be due to obliterative arterial disease. On the other hand, in the case reported by Wilson and Crouzon,[8] and called by them "senile combined sclerosis," in which there was very evident sclerosis in the posterior and lateral tracts, there were no marked vascular changes, and no anterior horn cell lesions.

Burr,[9] in 1901, emphasized the fact that many of the cases of partial palsies, vague rheumatic pains, and other dis-

turbances of senility, have their probable origin in central lesions due to the presence of diseased bloodvessels.

Naka, however, in a careful study of the pathological findings in 17 cases of senile dementia, states that he does not consider that the symptoms of spasticity, tremor, and increased reflexes have a sufficient explanation in the few changes which he was able to detect in the spinal cord and brain. He describes, however, thickening of bloodvessels, perivascular glia proliferation, and pigmentation and vacuolation of nerve cells.

That we are dealing, therefore, in cases such as those here reported, with symptoms or lesions the result simply of a deficient blood supply to the cells and fibers of the brain and cord, is most probable. Why the arteriosclerotic process should pick out in certain individuals the peripheral arteries, and in others only the central arteries, is as yet unexplained.

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1. Dejerine. Revue Neurol., 1906, p. 341.
2. Grasset. Revue Neurol., 1906, p. 433.
3. Sollier. Presse Médicale, 1906, p. 677.
4. Buzzard and Barnes. Rev. of Neur. and Psych., 1906.
5. Pic and Bonnamour. Rev. de Méd., 1904, p. 4.
6. Hirsch. Journ. of Nerv. and Ment. Dis., 1903.
7. Warrington and Owen. Rev. of Neur. and Psych., 1906.
8. Wilson and Crouzon. Rev. of Neur. and Psych., 1904.
9. Burr. Amer. Med., viii, 1904.

NOTES ON EXPERIMENTAL INOCULATIONS OF MONKEYS WITH GLANDS FROM CASES OF HODGKIN'S DISEASE.

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The following brief notes are reported because it has been impossible to find records in the literature of similar experiments. Except for Delbet,[1] who claimed to have produced general lymphomatous nodules in a dog by repeated intraperitoneal inoculations of cultures of a bacillus isolated from the blood and spleen of a case of lymphomatosis, and Cignozzi,[2] who states that he could produce a chronic atypical glandular tuberculosis in rabbits by the inoculation of emulsions of tumors from a case of Hodgkin's disease, no one has recorded any swellings of the lymph nodes which simulate the lesions of Hodgkin's disease after inoculation of the smaller laboratory animals with material from cases of Hodgkin's disease.

During the study of this condition, which has continued now for some time, it was decided to use monkeys for purposes of inoculation, with the idea that these animals might prove more suitable for experiment than rabbits or guinea-pigs. We have considered that our inoculations have given negative results, but since certain changes in the glands of the monkeys did take place it has seemed advisable to record the experiments.

The material for inoculation was obtained from cases of Hodgkin's disease at operation. Emulsions of glands were made carefully and under aseptic precautions in 0.85 per cent. salt solution. In most instances large doses of the fresh emulsions were injected under the skin of the chest and upper arm. These regions were chosen with the idea that the inoculated material would drain toward the axillary lymph glands.

In one instance small pieces of a gland were used instead of the emulsion, and later in the experiments the emulsion was fed to the monkeys as well as injected subcutaneously. Cultures on agar were always made from the emulsion before inoculation. In no instance was there a growth of bacteria. The three cases from which the glands were obtained presented the clinical symptoms of Hodgkin's disease, and the histological structure of the glands was perfectly typical.

The first monkey was inoculated on January 11, 1906, with 6 c.c. of fresh heavy emulsion of original glands from Case S. 401. Two days after the inoculation the swellings in the pectoral region and arm had entirely disappeared; there was no redness of the skin and the animal seemed well. On January 24, thirteen days after inoculation, the axillary and cervical glands were not palpable. No changes in the lymph glands were noted until February 9, almost a month after inoculation. On this date the following note was made:

"There is definite glandular enlargement. The axillary, inguinal, and cervical glands are swollen. In the axilla some of the glands feel the size of peas and are hard; in the right supraclavicular region they are small and shotty; in the inguinal region they are the size of peas." As the animal had not been carefully examined for some days prior to this date, it is possible that the glands might have been palpable before this. On February 14 the axillary glands on the left side were visible and were palpable along the pectoral muscle.

On February 16 a gland from the left axilla was removed

[1] Compt.-rend. de l'acad. des sciences, 1895, No. 24, p. 1373.
[2] Riforma Medica, 1906, xxii, 875.

under anesthesia for examination. Sections of one gland measured 6 mm. in diameter. Histological examination showed very extensive hyperplasia of the lymphoid elements. The follicles and lymph cords were greatly enlarged while the lymph sinuses were filled with cells and, except for the ones about the hilum, almost completely obliterated. Near the hilum the sinuses were much dilated and contained many large and small lymphocytes. In the peripheral sinuses there was some proliferation of the reticular endothelium. The germinal centres were of great size and many of the large pale cells showed karyokinetic figures. The periphery of the follicles and the cords were made up principally of small lymphocytes, though there were quite a number of large epithelioid cells, some almost of giant size, with single pale nuclei. Only one or two multinucleated giant cells were seen. Occasionally loose clumps of plasma cells were seen. The reticulum of the glands was not prominent. There were few or no polymorphonuclear leukocytes and no eosinophiles. The picture was that of marked simple lymphoid hyperplasia.

On February 19 the white blood cells were 15,300, and a differential count showed a proportion of cells which would be normal for human blood. The hemoglobin on February 28 was 75 per cent. The white blood cells, 13,100. A differential count showed polymorphonuclears 57 per cent.; small mononuclears, 32.6 per cent.; large mononuclears, 4.8 per cent.; transitionals, 3.4 per cent.; eosinophiles, 1.8 per cent., and basophiles, 0.4 per cent.

The monkey was examined from time to time, but the glands instead of increasing in size gradually diminished, until by May 4, 1906, the only glands which were definitely palpable were those in the groin. The monkey remained perfectly well and was finally used for a second inoculation.

Opportunity was offered, on September 8, 1906, to obtain fresh glands from another case of Hodgkin's disease (S. 567). Two small pieces of one of the glands removed at operation were planted subcutaneously in the chest of the monkey. In two days the wound had healed well, and very shortly afterward the lumps produced by the glands had disappeared entirely.

It was thought advisable to feed the glands to monkeys as well as inoculate the material subcutaneously, and, therefore, 5 c.c. of a thick emulsion of glands was fed to the monkey in his milk for four successive days.

For some weeks after inoculation the superficial lymph glands could not be felt. Finally on November 7, a marked general glandular enlargement was noticeable. The right axillary glands were particularly large, and by November 21 they felt almost the size of beans. The cervical glands and even the left axillary, in the region from which some of the glands were removed at the previous operation, were readily palpable, and by November 26 the glands in the left axilla felt as large as peas.

On November 27, 3 c.c. of the original salt solution emulsion of glands (S. 567), which had been kept on ice, were fed to the monkey, and on December 3 a piece of gland (S. 567), which had been kept in the thermostat in human blood serum, was given to the monkey in his food. On December 13, the general glandular enlargement seemed about the same, except that a marked fulness was seen beneath the jaw, and on palpation the submaxillary glands could readily be felt. The glands remained about the same size during December.

In hopes that repeated doses might have more effect than a single inoculation, emulsions from still a third case of Hodgkin's disease (S. 687) were inoculated subcutaneously on January 30, 1907, and 20 c.c. of the emulsion were fed to the monkey in his milk. On January 31 and February 4 subcutaneous inoculations were again made from the emulsion, which was kept in the ice box. This emulsion was cultured from time to time, but no growth of bacteria was ever obtained.

On February 21 the glands had not changed in size, and another subcutaneous dose of emulsion (S. 687) was given. By March 21 the glands had begun to decrease in size, and by April 12 they were definitely much smaller. On April 16 and 25 still further inoculations were made from the same material (S. 687). After this last inoculation an abscess developed in the left breast and the left axillary glands became somewhat larger, but the right axillary glands and cervical glands continued to decrease in size, and by June 14, 1907, none of the axillary or cervical glands were palpable.

This monkey certainly developed, after a single inoculation of an emulsion of glands from a case of Hodgkin's disease, a general glandular enlargement, which did not appear until several weeks after the inoculation had been made and which persisted for at least two months. A second single inoculation was attended by the same result, while after feeding the emulsion marked swelling of the submaxillary glands occurred. It is to be noted that although the glands remained about the same size, after the third inoculation of fresh material they decreased steadily in size during the repeated inoculations of old material, while an acute transitory swelling of only one group of glands followed the formation of the abscess in the left chest.

The second monkey, which received subcutaneous inoculations of glands from two of the above cases of Hodgkin's disease, showed practically the same changes as the first animal. A general glandular enlargement, not quite so marked as that in the first case, showed itself several weeks after the inoculation, remained for about two months, and then subsided.

It is difficult to say exactly what produced the general glandular enlargement in these two monkeys. It was probably not due to an infection of bacteria. The material was

very carefully prepared and cultures from it gave no growth of bacteria. It is very probable that the absorption of the comparatively large quantity of foreign material which was inoculated might bring about the changes in the lymph glands, but it is difficult to understand why, if this were so, the glands should continue to decrease in size after repeated injections of old material. On account of the expense and difficulty in obtaining monkeys, it was not possible to make any experiments to control this question. The histological picture o the excised glands was not that of Hodgkin's disease, so that the possibility of a mild and transient form of the affection having been produced in the monkeys must be rejected.

It is a great pleasure to thank Dr. Alfred Stengel for permission to keep the monkeys and make the inoculations in the Pepper Laboratory.

SOME DEFORMITIES AND INJURIES TO THE FACE AND JAWS OF THE FETUS IN UTERO, OR INCIDENT TO LABOR.[1]

By Robert H. Ivy, M.D.

While reports from time to time have been made of these deformities, and methods devised for their correction, yet very little has been said as to their actual causes. At first sight it may appear that the etiology is of minor importance as long as the deformity is recognized; yet, as I hope to show, the cause of the malformation is of great importance in considering the matter of correction. It may appear at first that this subject belongs rather to the specialist in oral surgery than to the general practitioner, yet most of these deformities that come to the oral surgeon or to the dentist for relief later in life should have been recognized by the general medical practitioner at the time of birth, at which time or shortly afterward the corrective treatment should have been instituted.

The first condition of which I wish to speak is congenital cleft palate. For a clear conception of the meaning of the term, it is necessary to know something of the development of the face and jaws in the embryo. Briefly outlined, the palate and the alveolar process of the maxillæ, or upper jaw bones, are formed from a lateral process on each side and frontonasal processes in front. A failure of these parts to unite explains the various kinds and degrees of deformity which constitute cleft palate. The two nasofrontal processes seldom fail to join, and therefore we rarely see a cleft of the palate extending in the median line to the anterior portion of the mouth. The two nasofrontal or premaxillary processes join to form the triangular intermaxillary bone, which contains the germs of the four anterior teeth, both temporary and permanent. Behind this bone, normally, the two lateral processes unite in the median line and form a V-shaped suture with it laterally. Therefore, in single cleft palate the cleft is found in the median line posteriorly, but when the intermaxillary bone is reached the cleft is deflected to one side, between the intermaxillary bone and the lateral process, and appears in the front of the mouth between the position of eruption of the lateral incisor and that of the canine tooth. In double cleft palate the cleft is single posteriorly, appearing in the median line, but divides on either side of the intermaxillary bone, and therefore appears as a double or Y-shaped cleft. In double cleft palate the intermaxillary bone is usually out of position, being tipped upward and forward, attached to the septum of the nose. Congenital cleft palate is found in varying degrees, the deformity being sometimes only partial, while at others it comprises the entire hard and soft palates.

Etiology. Every work on surgery vaguely states that cleft palate is perhaps brought about by imperfect development or interference with nutrition dependent upon injury or disease of the mother or fetus. This is too indefinite. Cryer has offered a much better explanation which is borne out by certain features of the deformity. He points out that there is usually little or no loss of tissue in congenital cleft palate, but that it is probably due to pressure of the mandible. The mandible, or lower jaw-bone, being formed first, is the natural modeller of the upper jaw, and may, by some undue pressure or position of the fetus in utero, be forced up between the formative processes of the maxillæ, preventing them from uniting, and thus producing the deformity. This explanation is borne out by the fact that in cleft palate the arch of the upper jaw is larger than and overlaps laterally that of the lower, which is not the case normally. Normally the lower arch is wider than the upper, by approximation of the bones the normal relations of the Furthermore, after the deformity has been properly corrected arches are obtained. It may be possible through investigation to determine what the disturbing conditions during pregnancy are which cause this undue pressure of the mandible, and the frequency of the deformity may be diminished by timely recognition of the predisposing factors.

Prognosis. In congenital cleft palate the prognosis for cure is usually good, if the child is otherwise healthy, and if operation is performed early. If left until adult life, opera-

[1] Read before the Barton Cooke Hirst Obstetrical Society of the University of Pennsylvania, November 9, 1906.

tion is out of the question when the cleft is of any great extent, and then it is that the dentist is called in to make mechanical appliances to correct the defect. In double cleft palate, where the intermaxillary bone is turned up out of position, the latter must very often be removed at operation, involving loss of the germs of the anterior teeth.

Age for Operation. The proper age for operation is as soon after birth as the child has become used to its surroundings. If its nourishment and general health are poor it is better to wait a few weeks and build up the infant before operation. The operative period may therefore be placed at from three weeks to three months after birth. The reasons for early operation are as follows: (1) The cleft causes interference with normal feeding, and the earlier this is corrected the better for the nourishment of the child. (2) The bones at this early age are plastic and can easily be bent and molded into shape. (3) The teeth have not erupted at this time and better access can therefore be had to the parts. (4) Surgical shock is believed to be less than later in life. (5) Speech will be more perfect if operation is performed before the patient has learned to talk. These conditions favoring early operation are advanced by Brophy, of Chicago, and are based upon 570 cases, 211 of which were under five months. When hare-lip is associated with cleft palate, the palate should be restored first, as the cleft in the lip greatly assists in rendering the parts accessible to the surgeon. The lip can be closed at a subsequent operation. Brophy's methods of operation give the best results in the early correction of cleft palate.

The next deformity to be considered is that known as inferior prognathism, by which is meant a projection or overlapping of the lower front teeth outside the upper. Observations have shown that the deformity is not merely a malposition of the teeth, but is primarily due to a forward position of the entire mandible, and that there is a subluxation of the condyle of the mandible on to the eminentia articularis of the temporal bone, instead of the condyle being back in its normal position in the anterior portion of the glenoid fossa. Examination of a skull in which inferior prognathism exists will show this. Cryer recently reported a case which should throw some light upon the cause of the subluxation at the temporomandibular joint. The patient had inferior prognathism. The *x*-rays showed subluxation of the condyle upon the eminentia articularis. The patient, who was himself a physician, when questioned as to his birth, stated that he had been a case of breech presentation. It is estimated that breech presentations occur in about 3 per cent. of all cases of labor. In various methods employed for delivery of the after-coming head in breech presentations, the finger of the accoucheur is placed in the child's mouth to make strong traction on the chin. Is it not reasonable to suppose that subluxation of the mandible may be caused by this procedure? In the rare cases of posterior rotation of the occiput in delivery of the after-coming head, the chin may be caught on the symphysis pubis, and subluxation be produced in this way. Profitable investigations could be made in the effort to trace a relation between methods of delivery of the after-coming head and inferior prognathism. At all events, it is the duty of the attending physician in a case of labor to examine the jaws of the child, and if the deformity has been produced, recognized by undue projection of the chin, to correct it immediately, pushing the condyles back into position. Later, if allowed to remain, it becomes impossible to reduce the dislocation. It is quite possible for this deformity to be produced by forceps in difficult labors.

Another deformity of the lower jaw occasionally seen in adults is absence of the normal angle of the mandible. The ramus in this case is nearly in a straight line with the body of the jaw, and the result is that only the back teeth occlude, leaving a space between the anterior upper and lower teeth when the mouth is shut. Absence of normal acuteness of the angle of the lower jaw may also be associated with the condition of forward bite of the lower teeth as just described. It is not an obliteration of the angle of the mandible so much as some interference with development, because there is scarcely any angle at birth in the normal subject. Investigation of cases of this character by L. S. Chilcote, of Bangor, Me., has shown that the deformity occurred in cases of difficult labor in which the jaws were subjected to undue pressure or in which the forceps were used. Though the condition cannot be corrected by the obstetrician when once produced, yet it may in some instances be prevented by special care in the application of the forceps, though of course consideration of the lives of mother and child must come first.

The last condition to be mentioned is fracture of the mandible during labor. I fail to find a single case of this accident reported. However, during my term as resident oral surgeon at the Philadelphia Hospital, I was called to see and treat a child in whom this injury had occurred. I did not obtain particulars as to the presentation and the course of the labor, except that forceps had been used in extracting the child and that the mother had died shortly afterward. The fracture was compound, and at the symphysis menti, which appears to be the most natural position for a fracture at this period of life. An impression of the lower jaw was taken and from it was made a vulcanite splint, which was held in position by means of wires passing from the splint in the mouth and fastened under the chin with a bandage. The child lived for three or four days with the splint in position but at the end of that time it unfortunately died from inanition, preventing further observation of the case.

The object of this paper has been to bring out a few of the conditions which if recognized by the attending physician in labor cases can usually be prevented or corrected at once, and which if allowed to remain uncorrected result in considerable disfigurement in after life.

BOOK REVIEWS.

Manual of Diseases of the Eye. By Charles H. May, M.D., Chief of Clinic and Instructor in Ophthalmology, College of Physicians and Surgeons, Medical Department, Columbia University, New York, 1890–1903; Ophthalmic Surgeon to the City Hospitals, Randall's Island, New York. Fifth edition, revised, with 362 original illustrations, 22 plates, 63 colored figures. New York: William Wood & Co., 1907.

The success of May's *Manual of Diseases of the Eye* is attested by the appearance of a fifth edition, the first edition having been issued in 1900, and by the fact that it has been translated into German, Italian, French, Dutch, and Spanish. The book has been kept well within the bounds of what it claims to be—a manual for students and general practitioners. Some new and better illustrations have been substituted and one new colored plate added. The plates illustrating the external diseases of the eye are exceptionally good reproductions of excellent colored sketches, such as are usually found only in much more expensive works. The methods of examination of the eye and of performing the ordinary operations are shown by means of photographs. Dr. May's experience in teaching at the College of Physicians and Surgeons in New York has taught him to avoid more than brief mention of the rarer conditions, and the importance of dwelling upon the more common diseases which the student and general practitioner should be able to recognize. The text has been brought up to date, and the book deserves hearty commendation as one of the best of its type on the medical bookseller's shelves. E. A. S.

The Harvey Lectures: Delivered under the Auspices of the Harvey Society of New York, 1905–1906. Philadelphia and London: J. B. Lippincott Co., 1906.

The Harvey Society was founded in October, 1905. Its primary object was to found a course of lectures which would bring the research laboratory workers of New York City into closer relation with the clinicians.

To quote the introductory remarks of Dr. Graham Lusk, to whose efforts the Society owes much of its success and who was its first president:

"Having in mind this idea of creating a common meeting ground, some of the laboratory workers in New York came together last spring and decided upon a new experiment. This experiment is the Harvey Society, founded for the diffusion of knowledge of the medical sciences through the medium of public lectures by men who are workers in the subjects presented. Dr. Theobald Smith has expressed our thought as regards the characters of these lectures. He writes: 'If I understand the scope of the Society rightly, such a lecture should be prepared with great care, from the broadest and most advanced outlook, while being at the same time purely instructive.'"

The volume under review is the first course of thirteen lectures delivered during the winter of 1905–1906. The list of lecturers contains many distinguished and representative names, including von Noorden, Novy, Park, Barker, Mendel, Minot, Clarence Webster, and Theobald Smith. The subjects of the lectures were chosen from almost every branch of medical sciences. We have not space to mention each in detail, but we note with a special interest those upon "Serum Therapy," by Park; "The Neurons," by Barker; "The Formation of Uric Acid," by Mendel, and "Some Phases of Tuberculosis," by Theobald Smith.

Too much cannot be said in praise of the object of the Society. If it rests with the scientific practitioner to raise the standard of medicine, and we are repeatedly told that it does, then there must be some method of correlating purely scientific and experimental work with the practice of medicine. This is the purpose of the Harvey Society, and we congratulate it upon the opening course of lectures.

The Society has a difficult road to travel, for it must steer a straight course, avoiding too popular addresses on the one hand and too abstractly scientific presentations on the other. However, with such men at the helm as those whose names appear on the list of officers and council, we have no fears but that the Society will richly fulfil its mission. J. D. S.

Nephritis. A Manual of the Diseases Commonly Called Nephritis or Bright's Disease and of Allied Disorders of the Kidneys. By Seelye W. Little, M.D. New York: The Grafton Press, 1907.

The author believes that nephritis is due almost entirely to the evils of civilization, especially the dietetic, and refers to the absence or extreme rarity of the disease in wild animals, and to its prevalence in rats after an excessive proteid diet (cheese), etc. He bases his treatment, therefore, upon the

adaptation of the "outrageous" environment to the "unfit" individual. From a pathological standpoint he recognizes only an active and a chronic form of nephritis, aside from infections, with varying degrees of vascular and parenchymatous change. In his definition he would include even more than Bright, for he considers transitory albuminuria, etc., even without demonstrable pathological changes, as merely a minor degree of "unfitness." More severe cases may, on the other hand, be made "fit" by modifying the environment. He classifies deleterious agents with reference to their effect upon the vascular tissues and the parenchyma. He follows von Noorden in restricting proteids, but thinks that the daily amount, even in the mildest cases, should not exceed 60 grams, whereas von Noorden allows nearly double that amount. This is of course based on Chittenden's work. Water should be restricted and milk, on account of its high proteid value, allowed only in small amounts.

The book offers little that is original, and the dietetic restrictions advised for severe cases seem extreme. There are occasional grammatical errors and ill-chosen or incorrect words, such as "humans." The numerous tables, derived from well-known sources, are convenient and the outline of treatment is, on the whole, rational. C. B. H.

Woman in Girlhood, Wifehood, Motherhood. Her Responsibilities and her Duties at all Periods of Life. A Guide in the Maintenance of Her Own Health and that of Her Children. By Myer Solis-Cohen, A.B., M.D., Instructor in Physical Diagnosis, University of Pennsylvania; Visiting Physician to the Hospital for Diseases of the Lungs, Chestnut Hill; Assistant Physician to the Philadelphia General Hospital; Physician to the Children's Dispensary of the Jewish Hospital, Philadelphia. Profusely illustrated with color plates, scientific drawings and half-tone engravings, with manikin chart printed in colors, and an index. Philadelphia, Chicago, Toronto: The John C. Winston Company.

Had the author confined himself to a consideration of those matters on the borderline of medicine for which there is a legitimate place, we can conceive that he might have produced a creditable and useful work. As it is, while there are many points of information valuable to woman, there is much else which could have profitably been omitted. It would be a truly remarkable fact if a book treating of so varied a subject as that indicated in the title, and embracing 418 pages in the telling, did not contain something of value.

Unfortunately the good is hopelessly jumbled amidst a mass of irrelevant facts and trivial details. We are told, for instance, that one should cultivate a kindly and cheerful disposition, as wrinkles are frequently caused by setting of the muscles of the face in certain lines that occur when the temper is bad and the disposition sullen or melancholic; that the teeth must not be used for cracking nuts; that a comb should be grasped between the thumb and first two fingers and that underclothing should always be removed on retiring.

On page 75 it is stated that, as sleep retards digestion, a person should not retire for two or three hours after a meal. The value of this advice is somewhat impaired, however, by the statement on page 86, that one should not go to bed hungry, but instead take some light simple food before retiring.

The book, as a whole, fails to recognize that society, as at present organized, has many divisions. Most of the advice given in regard to physical and mental recreation, such as horseback riding, golf, the collection of rare prints or old china is within reach of the well-to-do only. On the other hand, much of the advice pertaining to pregnancy, the puerperal period, and care of the child is gratuitous for this class, inasmuch as proper medical attention is employed. The title, as we have stated, allows of a very broad treatment of the subject. We are inclined to believe, however, that in matters pertaining to the color of a gown or the most suitable lullaby for the baby, the judgment of the woman herself may be safely trusted.

The admonition that when the child is ill a physician should be sent for, as valuable time is often lost by waiting too long, is certainly sound.

A more strict adherence to this dictum would have shortened the book very materially.

Illustrations unquestionably add to the value of a book if they aid in elucidating the text; otherwise they are superfluous. The illustrations under consideration do not in a single instance, so far as we have been able to discover, serve any good purpose, except in so far as they show how abominably wood-cuts can sometimes be done.

Apart from the statement that "colds" are acquired as the result of cold air striking the skin, the purely medical facts are in agreement with current views. The old adage, however, that a little knowledge is a dangerous thing, was never so true as when applied to books of this class.

H. R. M. L.

Conferences on the Moral Philosophy of Medicine. A Book for Medical Students and Young Physicians. Prepared by an American Physician. New York: Rebman & Co., 1907.

This manual of 368 pages consists in part of a commentary on the Hippocratic Oath and Law, the Code of Ethics of the

American Medical Association, Dr. Flint's Commentaries, etc., and in so far as it may lead to a wider familiarity with these classical standards, deserves the warmest commendation. The writer very properly emphasizes the debt we owe to Thomas Percival, whose work formed the basis of our national system. Besides the four chapters to which we have referred, constituting the nucleus of the work, there are preliminary chapters dealing with the physicians and medical schools of the past, with the rules of conduct which should guide the medical student, hospital interne, and young practising physician, and remarks on the value of cultivating the senses. The closing chapters treat of medical writing and speaking, etc., and are on the whole good though rather academic in their condemnation of such words as *practitioner*, especially as the author's fondness for long and involved sentences, high-sounding adjectives, and unusual words has led him into more patent errors. The form in which the book is cast, that of answers of an imaginary sponsor or an aspiring medical student, is tedious and without practical justification.

C. B. F.

UNIVERSITY OF PENNSYLVANIA

DEPARTMENT OF MEDICINE

FOUNDED IN 1765

This Medical School, the oldest in the United States, was founded in 1765 by Dr. John Morgan, who filled in it the first medical professorship created in America. In his opening "Discourse upon the Institution of Medical Schools in America," delivered in the College of Philadelphia on May 30, 1765, Dr. Morgan uttered these prophetic words: "Perhaps this medical institution, the first of its kind in America, though small in its beginning, may receive a constant increase of strength, and annually exert new vigor. It may collect a number of young persons, of more than ordinary abilities, and so improve their knowledge as to spread its reputation to distant parts. By sending these abroad duly qualified, or by exciting an emulation amongst men of parts and literature, it may give birth to other useful institutions of a similar nature, or occasional rise, by its example to numerous societies of different kinds, calculated to spread the light of knowledge through the whole American continent, wherever inhabited."

Through Dr. Morgan, the pupil of Hunter in London and of Cullen in Edinburgh, the graduates of this school take a just pride in regarding it as the lineal descendant of the best medical schools of Great Britain in the last century. To Dr. Morgan was soon joined another pupil of Cullen, Dr. William Shippen, as Professor of Anatomy and Surgery, thus forming another tie of relationship to the celebrated University of Edinburgh, whose methods of instruction were substantially adopted here. In the next year Dr. Adam Kuhn was added as Professor of Botany and Materia Medica; and in June, 1768, a "Commencement was held," at which medical honors were bestowed, the first in point of time in America. In 1769, Dr. Benjamin Rush was elected Professor of Chemistry, while Dr. Thomas Bond, one of the trustees of the College of Philadelphia, delivered lectures on Clinical Medicine in the Pennsylvania Hospital.

To the faculty thus composed of Morgan, Shippen, Bond, Kuhn, and Rush have succeeded, at various times, professors whose reputation has been national, such as Wistar, Barton, Physick, Chapman, Hare, Gibson Horner, Dewees, Jackson, George B. Wood, Hodge, James B. Rogers, Carson, R. E. Rogers, Leidy, Henry H. Smith, Pepper, Francis Gurney Smith, Stillé, D. Hayes Agnew, Goodell, W. Pepper, Jr., and Ashhurst.

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THE LIVER IN ANTIQUITY AND THE BEGINNINGS OF ANATOMY.[1]

By Morris Jastrow, Jr., Ph.D.,
Professor of Semitic Languages at the University of Pennsylvania.

Medicine—as is well known—is an offshoot of religion. The first teachers of mankind were priests, and included in the functions of the priest in primitive conditions and in early civilizations, we find on the one hand, that of lawgiver and judge, and on the other, that of diviner and healer of diseases. All knowledge in the infancy of civilization, as it was acquired, was put in the service of the cult. There was no science outside of religion, and even the arts—music, dancing, painting, sculpture—were in their origin allied to religion, and only gradually cut loose from being merely parts of religious ceremonialism or adjuncts in the worship of the gods.

The predecessor of the physician as healer is the priest as exorciser, engaged in the endeavor to drive out of the human body the demons who were regarded as the source of disease. These "demons"—invisible to the naked eye—were the precursors of the modern "germs" and "microbes," while the incantations recited by the priests are the early equivalents of the physician's prescriptions. There were different incantations for different diseases; and they were as mysterious to the masses as are the mystic formulas of the modern physician to the bewildered, yet trusting patient. Indeed, their mysterious character added to the power supposed to reside in the incantations for driving the demons away. Medicinal remedies accompanied the recital of the incantations, but despite the considerable progress made by such nations of hoary antiquity as the Egyptians and Babylonians in the diagnosis and treatment of common diseases, leading in time to the development of an extensive pharmacology, so long as the cure of disease rested with the priests, the recital of sacred formulas, together with rites that may be conveniently grouped under the head of sympathetic magic, was regarded as equally essential with the taking of the prescribed remedies.[2]

Complementary to the function of the priest as exorciser in driving ills out of the body, we find, in primitive times, the priest acting as diviner in order to forestall by his ability and skill in forecasting the future, the ills and misfortunes threatening the country or the individual. Divination in some of its aspects might be called the "preventive medicine" of antiquity, and if the priest as exorciser represents the source of practical medicine, it is through divination that we are led to the beginnings of anatomy—as an adjunct to medicine.

Through the application of a curious theory as to the seat of life in men and animals, the priest as diviner becomes a student of animal anatomy.

Divination covers a wide scope in all religions of antiquity, both primitive and advanced. The desire to tear the veil from the face of the unknown future is an impelling factor in all religions, which is accentuated in the more primitive cults by the fear of the unknown. We may distinguish in divination two broad divisions, which may be designated as involuntary and voluntary. Involuntary divination deals with the endeavor to interpret signs that are forced on our attention, that come as it were independently of our volition, and that, therefore, were regarded as fraught with some special significance. To this class belong dreams, unusual or peculiar occurrences, the birth of monstrosities among men or animals, and all the little mishaps or specially significant incidents of life. Most important of all, however, are the signs furnished by the phenomena of the heavens, the movements of the planets, the phases of the moon, the action of the sun in its course along the heavens, and, naturally, such occurrences as storms, the play of lightning, rain out of season, eclipses, and so forth. From the observation of the heavenly bodies there arose the science of astrology, based on the belief that the movements of the planets and stars, which were identified with specific gods, represented the activity of the gods in preparing the events that were at their bidding to take place on earth. There was supposed to exist a complete parallel between what occurred in the heavens and what subsequently manifested itself on earth. Hence, the theory which, when once developed, retained its hold tenaciously upon mankind down to the threshold of modern days, that if one could read the stars one would know what the future had in store.

By voluntary divination I mean the deliberate seeking for some sign or for signs that by a more or less developed system of interpretation would furnish an answer to an inquiry with regard to the future. The sign in question is not one that comes involuntarily, forced on one's attention through circumstances beyond our control, but which is deliberately sought out. We might call the signs of involuntary divination, portents, and those of voluntary divination, omens. Thus, when the question arises whether a king should lead his

[1] An address before the College of Physicians of Philadelphia, November 6, 1907.

[2] As a survival of the primitive belief in the power supposed to reside in sacred words and formulas, it is said that it is not uncommon for the *fellahs* of Egypt, when ill to swallow the written prescription as well as the medicinal dose.

army to battle on a certain day, and in order to reach a decision, arrows are thrown before the statue or symbol of the patron deity[1] and according as they fall, the priest would read the answer of the god—we have an instance of the second division of divination lore. Taking a bowl of water into which some drops of oil are poured, and then noting the action of the oil bubbles, would be another instance of voluntary divination.[2]

The most common method of voluntary divination widespread in antiquity was through the inspection of a sacrificial animal. There was one organ of the animal specifically singled out as a means of divining the future, namely, the liver. The custom of divining through the liver of an animal specially set aside for the purpose belongs to the primitive stage of religion, as is vouched for by its occurrence among the native population of Borneo, Burma, Uganda, and elsewhere.[3] In Borneo a pig is the ordinary animal of sacrifice, in Burma a fowl or a pig is used, while in Uganda the livers of goats are the ones usually chosen. The custom was, however, carried over into higher stages of civilization, and we find it as an integral part of the cult among the Babylonians and Etruscans,[4] as well as among the Greeks and Romans,[5] while traces of the theory underlying the rite are encountered among the Hebrews and Arabs, as well as in India and China.[6]

To be sure, among the Romans other organs, as heart and lungs, were examined besides the liver, but this appears to have been *in later days*,[7] and even then the references to divination through the inspection of the heart are few, while the references to the lungs are still rarer.[8] As a matter of fact, although the Greek and Roman historians and essayists, when speaking of divination, make use of the general terms *iera* ("victims") or *iereia*, "sacred parts," and *exta*, "entrails," respectively,[1] when specific instances of divination through the inspection of the sacrificial animal are referred to, they always involve parts of the liver or markings on the liver or they refer to the gall-bladder, which, lying on the liver, was regarded as an integral part of it. We may, therefore, dismiss the consideration of other organs and bear in mind once for all that the liver is, as Bouché-Leclercq puts it, "the organ of revelation *par excellence*."[2]

The theory underlying this curious rite is a very simple one. The liver was in early days universally regarded as the central vital organ in the animal, the seat of all forms of mental and emotional activity, or, in other words, as the seat of the soul. We have been accustomed to think that the heart was, among ancient nations, looked upon as the seat of the soul, but while this is true for Greece, Rome, and India, as well as for the Hebrews at a certain stage of culture, even in these civilizations there was an earlier period in which that distinction was accorded to the liver. A trace of this earlier view is to be found in the use of the word for liver in Greek (*hēpar*), which is applied in Greek poetry as the word "heart" is in prose.[3] So when a person is mortally wounded, he is spoken of as "struck in the liver." The punishment of Prometheus, whose liver is gnawed by a vulture, also rests on this primitive view. The liver is singled out because it is the seat of life. In Hebrew poetry, likewise, the word for liver (*kabed*) is used synonymously with the word for soul (*nefesh*), and even as late as the days of Mohammed the story is told that on an occasion of great sorrow the prophet wept all night "as though his liver would crack," where we would say, "as though his heart would break."[4]

This position accorded to the liver in antiquity must not be confounded with the current popular notion which supposes the liver to be the source of the lower emotions, as jealousy, malignity, ill-humor, or timidity. Such a view represents the degradation of the liver from the high position it once occupied as the seat of the intellect and of *all* emotions, the higher ones—as love and courage—as well as the lower ones. The liver as the seat of the soul becomes practically identical with what, in the common view, was regarded as the soul. It is to this stage that the practice of divination through the liver of the sacrificial animal reverts.

The question may, however, be asked, How came people

[1] Practised among the ancient Arabs.

[2] Found in Babylonia and among the Persians. See Hunger, Beobachtungen bei den Babyloniern (Leipzig, 1903). The "cup" of Joseph described in Genesis 44: 2, 5, and 15, as used for divination purposes, falls within the category of "oil and water" divination. It may be of interest to note that "oil" divination is still practised at the present time. I am told that among certain classes of Italians—more especially among those from Sicily—in Philadelphia, after a doctor has been called in and prescribed for a patient, the members of the family take a bowl of water, pour some oil in it, and if the bubbles pass to the right it is believed that the patient will recover, but if they pass to the left that he will die.

[3] See the references in Blecher, De Extispicio (Giessen, 1905), pp. 73–74, and in the author's Religion Babyloniens und Assyriens, ii, p. 216.

[4] For the Babylonians, the details, with copious translations of "liver" divination texts, will be found in the author's Religion Babyloniens und Assyriens, ii, chapter xx; for the Etruscans, see Bouché-Leclerq Histoire de la Divination dans l'Antiquité, iv, p. 68 seq., and Thulin, Etruskische Disciplin, ii, (Göteberg, 1906).

[5] For the Greeks and Romans, see Blecher, De Extispicio.

[6] See the author's work, ii, pp. 217 and 231

[7] Pliny, in his Natural History, xi, §71, states that the first time that the heart was examined in a divination rite by the Roman soothsayers occurred in the 126th Olympiad, which corresponds to the year 274 B. C.

[8] Thulin, in his Etruskische Disciplin, ii, p. 23, gives only six references to divination through the heart and only three references to the lung—all of them late and of an indirect character.

[1] See the passages in Blecher, De Extispicio, pp. 3–22.

[2] Histoire de la Divination, iv, p. 68.

[3] See Stephanus, Thesaurus Linguæ Græcæ, under *hēpar*. See for Hebrew usage, Lam. 2 : 11 and Proverbs 7: 23.

[4] My friend and colleague, Prof. Torrey, of Yale University, kindly called my attention to this reference in Arabic literature. See Krehl, Recueil des Traditions Musulmanes, ii, p. 156; Torrey, Selections from the Sahihh of Buchari, p. 38.

to the belief that through the soul of an animal the course of future events could be determined? A brief consideration of the views held in antiquity as to the nature of vitality and as to the nature of gods will make the connection between the liver and divination clear. Life of all kind was held as sacred by ancient nations, and was everywhere regarded as due to the gods. To such an extent did this view prevail that the manifestations of life, whether among animals, trees, or rivers, were often identified with the gods. The distinction between the symbol and the thing symbolized was not sharply maintained; hence, the animal becomes the manifestation of the god; the tree, which also gives evidence of some form of life within it, is a local habitation for a god; while the river is, as one views it, the habitat of the god or the god himself.[1]

The life or soul, as the seat of life, in the sacrificial animal is, therefore, the divine element in the animal, and the god in accepting the animal, which is involved in the act of bringing it as an offering to a god, identifies himself with the animal —becomes, as it were, one with it. The life in the animal is a reflection of his own life, and since the fate of men rests with the gods, if one can succeed in entering into the mind of a god, and thus ascertain what he purposes to do, the key for the solution of the problem as to what the future has in store will have been found. The liver being the centre of vitality—the seat of the mind, therefore, as well as of the emotions—it becomes in the case of the sacrificial animal, either directly identical with the mind of the god who accepts the animal, or, at all events, a mirror in which the god's mind is reflected; or, to use another figure, a watch regulated to be in sympathetic and perfect accord with a second watch. If, therefore, one can read the liver of the sacrificial animal, one enters, as it were, into the workshop of the divine will.

Now, whether one accepts the theory here set forth or not, so much is certain that we must look for some *rational* view underlying a custom that, in the case, *e. g.*, of Babylonia and Assyria, prevailed for a period of about 3000 years. The system devised for the interpretation of signs to be seen on the liver would never have survived during so long a period without some theory that commended itself to a people of such notable achievements as the Babylonians and Assyrians. A system built up on a foundation of caprice and arbitrariness would not have lasted. It would either have had its outcome in deliberate fraud or it would have defeated its ends by revealing in time its own absurdities.

We are now approaching the point of interest to students of the history of medicine in this widespread rite of divining the future through the liver. The rite led in Babylonia, and no doubt, also among so highly civilized a people as the Etruscans to the *anatomical study* of the liver. Confining ourselves to Babylonia and Assyria, where the sources at our disposal are now very copious, and where divination through the liver can be traced back to the most ancient period of Babylonian history known to us—c. 3000 B. C.—we find this anatomical study betraying all the external symptoms of a scientific or quasiscientific study. The animal ordinarily used for sacrifice was the sheep, and we are now in a position to state that the study of anatomy begins with the analysis of the sheep's liver as early at least as 3000 B. C. The parts of the liver to which, in divination rites, special attention was paid were the various lobes, the gall-bladder, the portal vein, the gate of the liver, the two appendages to the upper lobe (known as the *lobus caudatus*),[1] and to the markings on the liver lobes, due to the traces on the surface of the liver of the subsidiary gall-ducts that gather the gall from the liver into the gall-bladder and to the subsidiary vein ducts distributing the blood from the large portal vein through the liver. No two livers, naturally, presented the same phenomena—as little as two leaves of a tree—and the innumerable variations in the character of the lobes, in the gall-bladder and various ducts, and in the markings on the liver furnished a boundless field across which the fancy of the divining priests could roam at will.

The Babylonian priests, thus led to the study of animal anatomy, prepared clay models of the sheep's liver to be used as object lessons for the instruction in the temple schools to the aspirants to the priesthood. A model of this kind now in the British Museum, and belonging at one time probably to the school in the temple of Marduk, in the city of Babylon, dates from the period of Hammurabi (c. 2000 B. C.).[2] It shows the parts of the liver distinguished, and from the omen texts themselves we learn the designations given to these parts. Let us see how far this anatomical study went. The right and left lobes were naturally distinguished, and, corresponding to the modern terms *lobus dexter* and *lobus sinister*, they were designated as "the right wing of the liver" and "the left wing of the liver" respectively. Whether the right lobe was further separated by them, as in modern anatomy, by the groove in which the gall-bladder lies (*fossa sagittalis dextra* or *fossa vesicæ felleæ*) into the *lobus dexter* proper and the *lobus quadratus* is uncertain, but it would seem not, though the omen texts do furnish a designation for this groove, which was called "the river of the edge of the liver," to distinguish it from the umbilical groove (*fossa sagittalis sinistra* or *fossa venæ umbilicalis*) separating the left

[1] See chapters xv and xvii in Jevon's Introduction to the History of Religions (London, 1896).

[1] Formerly known as the *lobus Spiegel*. I follow the nomenclature proposed by Stieda for the various parts of the liver in his paper on "Die aeltesten bildlichen Darstellungen der Leber," in Bonnet-Merkel, Anatomische Hefte, Band 15, p. 695.

[2] Published in Cuneiform Texts from Babylonian Tablets, etc., in the British Museum, Part 6 (London, 1898), Pl. 1. The illustration is also found in Boissier, Note sur un monument Babylonian se rapportant à l'Extispicine (Geneva, 1899), and in Thulin, Etruskische Disciplin, ii (Gotcberg, 1906), Pl. II, as well as in Stieda's article referred to in the preceding note. (See Fig. 1.)

lobe from the *lobus quadratus*, and which was called the "river of the liver," without further specification. The fourth lobe at the upper part of the liver known as the *lobus caudatus* was appropriately termed from its position "the middle of the liver." Attached to this lobe are two appendages, a larger one at the right end, for which Stieda proposes the name *processus pyramidalis*, while the smaller at the left end is called the *processus papillaris*. The larger appendix has the distinct outlines of a finger, and was, therefore, called "the finger of the liver," or, more fully, "the finger of the middle lobe,"[1] while the smaller one was designated by a sign which

FIG. 1.—Babylonian clay model of sheep's liver with a divination text of the period of Hammurabi (c. 2000 B.C.)

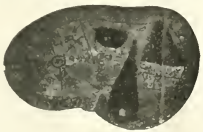

FIG. 2. Bronze model of liver found near Piacenza in 1877, used in Etruscan divination (c. 3d century B.C.).

appears to have the meaning of "offspring" or "small." The gall-bladder (*vesica*) bore the very appropriate name of "the bitter" part, the cystic or biliary duct (*ductus cysticus*), into which the gall-bladder issues, was designated by a sign which in all probabilities means the *pe'ais*, while the hepatic duct (*ductus hepaticus*), into which the biliary duct passes to the left, was called "the outlet." The designation is interesting as showing that the Babylonians believed that the gall passed from the gall-bladder into the cystic and hepatic ducts, whereas, as a matter of fact, the hepatic duct is really an "inlet," collecting the gall passing through the subsidiary ducts from various parts of the liver, to be finally brought into the gall-bladder for purification. On the right side the biliary duct leads to the common bile duct (*ductus choledochus*).

FIG. 3. Diagram of sheep's liver, showing modern anatomical terms and their Babylonian equivalents.

The juncture forms a "yoke," which, accordingly, was the name given to this common bile duct. By the side of the hepatic duct lies the great portal vein (*vena portæ*), which the Babylonians called the "strong." It is not certain whether they specially distinguished the subsidiary veins, though a term "splits" frequently occurring in the omen texts may be intended as a description of these ducts. On the other hand, the subsidiary hepatic ducts are distinctly referred to and appropriately termed "branches." Lastly, there is the transverse fissure of the liver above the left lobe, known as the liver gate (*porte hepatis*), and in which the hepatic duct and the portal vein wholly or in part lie. The Babylonians called this depression on the surface of the liver the "crucible." For the *vena cava* connecting the liver with the heart I have not found the Babylonian designation, and

[1] It is of interest to note that in the Pentateuchal codes a phrase which in literal translation reads "that which hangs over the liver," and which is generally rendered the "caul above the liver," occurs ten times (Exodus 29: 13 and 22; Leviticus 3: 4, 10, 15; 7: 4; 8: 16 and 25; 9: 10 and 19. It is the Hebrew equivalent for this "finger" of the liver. The proof for this was furnished by Prof. George F. Moore, in a paper published in the "Noeldeke Festschrift," p. 761 seq. The Rabbinical tradition correctly interpreted the phrase, as is indicated by the term "finger of the liver," used to describe this appendix in the later Hebrew literature. According to the passages in the Pentateuchal codes referred to, this part of the liver was to be burned in the case of the various kinds of animal sacrifices—sin offerings, guilt offerings, and peace offerings—and it seems a plausible conclusion that the reason for this ordinance was that the burning might serve as a symbolic protest against the use of the liver for divination purposes. The theory underlying animal sacrifice in the Old Testament is, that it serves as a tribute to the Deity or as an atonement, and since the spirit of all the Pentateuchal codes is firmly opposed to sorcery, incantations, and divination of all kinds, it is not surprising to encounter a provision which is intended to be a protest against the Babylonian view, that made sacrifice a means for securing the aid of a god in divining the future.

it is doubtful whether it was taken into consideration at all. So much for the anatomical side of "liver" divination. (See Fig. 3.)

The play of fancy begins even before we reach the system devised for the interpretation of phenomena observed on the liver. The markings on the liver to which reference has already been made were combined to form all kinds of fantastic figures. The more simple of these markings were called "roads;" others, which appeared to be depressions, were known as "holes," but even more commonly these markings were fancifully combined to form various kinds of weapons or parts of weapons. The gods of Babylonia and Assyria are often symbolized on so-called boundary stones by weapons associated with them,[1] and, because of this association, markings on the liver that seemed to bear a resemblance to such weapons were connected with various gods and goddesses, and an interpretation was given to these markings which accorded with the attributes of the deity in question. A marking, *e. g.*, connected with the weapon of Ninib—a storm god—was interpreted as pointing to some event in which Ninib would manifest his power, either as an ally or as a hostile force; a weapon associated with Ura—the plague god—would point to sickness; the weapon of Ishtar—the chief goddess of the Babylonian-Assyrian pantheon—would prognosticate, according to further indications, the favorable or unfavorable activity of that goddess; and so through the long list of the pantheon.

In order to reach a decision as an answer to any given question, all the signs and phenomena noted on the liver were recorded, the meaning of each determined whether it was favorable or unfavorable, and then, by a combination of the prognostications a conclusion was reached whether a proposed undertaking, a battle, a journey, a proposed appointment to an official post should be risked, or whether the outcome of a disease or an occurrence of some kind would be favorable or unfavorable. The general principle underlying the elaborate system of interpretation that was in the course of time developed, rested on a more or less natural and logical association of ideas. If a certain sign on the right side was favorable, the same sign on the left side was usually unfavorable. Most of the interpretations bore on public events, but could be applied also to private affairs. Thus, if the gall-bladder was swollen on the right side, it pointed to an increase in the strength of the king's army, and was, therefore, interpreted as a favorable sign in general; while the swelling on the left side prognosticated the success of the enemy, and was, therefore, an unfavorable sign. If the gall-bladder lay tightly embedded in the gall-bladder groove, it meant, if on the right side, that the king's army would be in the firm grasp of the enemy, and, therefore, to be regarded as an unfavorable symptom; if, however, the left side of the gall-bladder was tight, that the enemy would be kept as a prisoner, and, therefore, a favorable symptom for the king's army. If the biliary duct was long, it pointed to long life; if the hepatic duct was well enclosed in the gate of the liver, it meant success in battle; if, however, it lay above and beyond the hepatic duct, it indicated a position exposed to the attack of the enemy. If the finger-shaped appendix (*processus pyramidalis*) was broad, it was interpreted as joy; if it was small, while the other appendix—usually small—was large, it pointed to an inversion of the natural order. The son would be mightier than the father, the servant would prevail against his master; *i. e.*, in general that the "small" would be great and the "great" submit to the "small." Gall-stones, designated as "knots," are also not infrequently mentioned in the divination texts, and in connection with other symptoms are either favorable or unfavorable. These few examples illustrating the general character of the system of interpretation will suffice for our purposes. It will be apparent how in this way, on the basis of an endless series of examinations of the livers of sacrificial animals, an almost endless series of signs and phenomena would arise, while the interpretations based on the general principle here set forth, and reinforced by the records of the actual events that followed on the occasions when the auspices were taken, would grow in equal proportion to the observations made. The signs and the interpretations were gathered by the scribes attached to the various temples into hand- and reference-books, which would serve the double purpose of guides for the interpretation of omens, and of text-books for instruction in the temple schools. One can easily imagine the huge proportions assumed by the system of hepatoscopy in the course of many centuries.

That practically the same system was followed by the Etruscans, Greeks, and Romans is apparent from the references in Greek and Roman writers. For the Etruscans, we have as confirmatory evidence of these references the model of a sheep's liver in bronze, dating from about the third century B. C., and which was found near Piacenza (Italy) in 1877.[1] On this bronze liver the same parts of the liver as in the case of the Babylonian clay model are indicated, even to the markings on the livers, which are somewhat conventionally represented by lines converging to a single focus. Indeed, the resemblance of this bronze liver of Etruria to the Babylonian counterpart is so close that it is hard to resist the conclusion of a connection between the two. There

[1] See Dr. W. J. Hincke, "A Boundary Stone from Nippur of the Days of Nebuchadnezzar I," Introduction (Phila., 1907).

[1] Now in the Museo Civico at Piacenza. Numerous monographs have been written about this remarkable object, the latest being a summary of twenty-five years of study of it by Prof. Korte, "Die Bronzeleber von Piacenza" (Mittheilungen des Deutsch-Archaeologischen Instituts, Romische abtheilung Band XX, pp. 348-379). Illustrations of it will be found in the monographs of Bleeker, Thulin, and Korte, above referred to. See also Thulin, Die Götter des Martianus Cappella und die Bronzeleber von Piacenza (Giessen, 1906). (See Fig. 2)

are many indications which point to the East as the home of the Etruscans, and the development of elaborate systems of hepatoscopy among both Babylonians and Etruscans would seem to be a definite link connecting the two civilizations; and since the Babylonian culture is by far the older of the two, it would seem to be a further reasonable inference that the Etruscan system is dependent upon the Babylonian. At all events, it is the development of an elaborate system of interpretation that has in both instances brought about the incorporation of hepatoscopy as an integral part of the religious cult, and that led to the continuance of the rite throughout all the changes of an advanced and advancing civilization. Without this system, liver divination would have died out, or at best survived as a superstition, *i. e.*, as a non-official popular custom, as it died out in India, China, Judea, and other countries with the advance from primitive culture to higher planes of belief and religious practice.

Our knowledge of Greek and Roman hepatoscopy is unfortunately limited to incidental notices. We have not, as in the case of Babylonia and Assyria, copious omen collections and omen reports furnishing both the signs observed and the interpretations offered. That handbooks and such collections existed among the Romans we know from references in Livy, Cicero, and various other writers,[1] but they have not been preserved. We also have the direct evidence in Roman writers that the Romans took over their system of divination through the liver from the Etruscans, and up to a late day the augurs in Rome were generally imported from Etruria.[2] In the case of Greek hepatoscopy, the question whether it also reverts to Etruscan origin is still an open one, with indications rather in favor of assuming a direct connection with Babylonia and not through the mediation of Etruscans.[3] The anatomical nomenclature is not the same for Greek and Roman hepatoscopy; so, *e. g.*, the *processus pyramidalis*—the finger-shaped appendix at the right end of the caudate lobe—is known as ὁ λοβός, "the lobe" *par excellence* in Greek,[4] no doubt because of the important part that it played in divination; whereas, the Romans designated it as *caput jecoris*, "the head of the liver," which, likewise, points to the dominant position of that appendix in the system of interpretation. More important, however, is the proof furnished from references in Greek and Roman writers that the parts and signs on the liver that enter into consideration are the same as in Babylonian hepatoscopy. Thus, in the passage in the Prometheus of Æschylus (line 495 seq.), in which Prometheus, recounting among the benefits that he conferred on mankind the art of divining through the sacrificial animal, the gall-bladder and the *processus pyramidalis* are singled out as particularly significant, while in a passage in the Elektra of Euripides (lines 826 seq.) the "gate of the liver"[1] is added. As in Babylonia, the enlarged character of the *processus pyramidalis*, so that it sometimes appeared to be "double," was a good sign, pointing to enlargement of power,[2] while the absence, real or apparent, of this appendix was an unfavorable symptom. So, again, the "black" color of the gall-bladder was an unfavorable sign, just as in Babylonian omen texts the "black" color always involved an unfavorable augury.[3] Finally, from glosses in Hesychius we learn that the Greeks, and presumably, therefore, also the Etruscans and Romans, gave fanciful designations, as did the Babylonians, to the markings on the liver. Among these designations we find terms like "twins"—probably for a double loop—"receptacle," "tongue," "hindrance," "opponent." The terms include one that may be translated "knot," and which involuntarily suggests the Babylonian designation of "gallstone" above pointed out.[4] The term "river" also occurs in the list, which reminds one of the Babylonian term for the two grooves of the liver. From Hesychius we also know that the four lobes of the liver were designated by fanciful terms, namely, "table," "hearth," "knife," and "driver." These terms were transferred from hepatoscopy into human anatomy and continued in use to the eighth century of our era.[5] Such terms, just because of their fanciful character, were well adapted for use in the divination rites, where the association of ideas was to so large an extent dependent upon supposed resemblances of parts of the liver and signs on the liver to certain objects. The origin of these terms is thus revealed, and, incidentally, they furnish a further proof for the thesis here maintained that the study of anatomy actually begins with the importance attached in divination to the liver of the animal offered up as a sacrifice.

Before leaving the subject, let me point out how, with the addition of other organs to be examined for the purpose of divining the future through them, the basis upon which the entire system of hepatoscopy rested was destroyed. I referred in the early part of this paper to the theory underlying hepatoscopy everywhere, namely, the belief, which at one time was general, that the liver was the central vital organ and as such the seat of the soul. As long as anatomy was attached to divination this view continued to be held, but when medicine cut loose from the leading-strings of religious observances,

[1] See the references collected by Thulin, Etruskische Disciplin, i, pp. 1–12.

[2] Cicero, De Divinatione, i, 2. See Thulin, l. c., ii, p. 1.

[3] See the author's Religion Babyloniens und Assyriens, ii, p. 320, note 3.

[4] In the Greek translation of the passages in the Pentateuchal codes above referred to, the Hebrew term for *processus pyramidalis* is correctly rendered as ὁ λοβός.

[1] *pulai*, "gates," to which the modern term *portæ hepatis* reverts.

[2] See the examples in Thulin, Etruskische Disciplin, ii, p. 31.

[3] For examples, see Jastrow, Religion Babyloniens und Assyriens, ii, p. 341, note 7.

[4] See above, page 242.

[5] They occur in Theophilus Protospathius' work, De Fabrica humani corporis, ii, 13 (p. 81 of Greenhill's edition, London).

anatomy, too, became an independent science, and progress in the study led to assigning to the heart a much more important place than it had hitherto held in the common mind. As a result, the view gradually took shape which gave to the heart the place once occupied by the liver. This stage is reflected in the *current* use of the word heart in Greek prose, in Latin, in Hebrew, as well as in India[1] and elsewhere, and to such an extent, indeed, that, as we have seen, only sporadic traces of the earlier view survived. In this second stage the heart is not merely the seat of the emotions, but of the intellect as well. In the Old Testament, *e. g.* the word *lebh* is not only used in this way, but is frequently employed as the synonym of *nephesh* "soul, life," etc. Even in modern languages there are survivals of this second stage in the endeavor to localize the soul in some organ. We still speak of learning something "by heart," where heart is clearly used in the sense of "intellect." Similarly, in *recordare*, in the sense of "recalling," it is the heart which is assumed to be the seat of the intellectual activity involved. Ennius, who spoke three languages, is described as having "three hearts;" and more the like.[2]

It was because of the general prevalence of this view that the Romans—and perhaps also the Greeks—added the heart to the liver in the inspection of the sacrificial animal for the purpose of divining the future; and this step being once taken, it was naturally followed by taking also the lungs and the "internals" in general into consideration. In taking this step, however, the basis of the rite was destroyed. The underlying theory of hepatoscopy being, as we have seen, the supposition that the liver was the divine organ in the sacrificial animal, which took on, as it were, the character of the "soul" of the deity to whom the animal was offered the *rationale* of the rite disappeared with the abandonment of the theory, and it is a common phenomenon in the history of religion that a religious ceremony degenerates into a meaningless superstition, and even issues in fraud, if the substratum on which it rests is disturbed. In Babylonia and Assyria, where for a period of several thousand years the liver was consistently employed as the sole organ of divination, there are no traces that the rite fell into decay or was abused by the priests. Indeed, we are rather astonished at the candor with which unfavorable decisions on the basis of the inspection of the liver of the sacrificial animal are rendered, and there are numerous instances of endeavors to ensure for one's self the correctness of the answer to the question propounded by repeating the inspection two or three times. If, therefore, among the Romans we find suspicion of the integrity of the priests issuing in the open declaration of deliberate deception, as instanced in the famous observation of Cato, that in his days two augurs could not meet without laughing,[1] we are justified in tracing this degeneration of the rite to the destruction of its basis by adding other organs to the liver. If the liver was not the seat of the soul, there was no reason for the rite, and with the disappearance of this belief it is not surprising to find such a strategy as is recorded in several classical writers of a ruler who, in order to encourage his soldiers to give battle, engaged a priest to write the words "victory to the king" on the palm of his hand; with the letters reversed, to put the smooth side of the liver of the sacrificial animal on his hand, make a pretence of examining it, and then to hold up the liver in the sight of the army with the miraculous inscription.[2] The tale well illustrates the degradation of the rite after the belief upon which it rested had disappeared.

The advance in the study of anatomy marked by Hippocrates (460–351 B. C.) and his school led to the full recognition of the functions of the brain, and in consequence we reach a third stage in which, owing to the predominating significance of intellectual functions in human existence, the disposition became pronounced to place the seat of life and even the soul in the brain. To be sure, Hippocrates himself betrays a trace of older views in making the liver the seat of the blood[3] and since blood was always identified with life, this was merely a more scientific manner of stating that the liver was the vital organ *par excellence*. It is also worthy of note that Aristotle[4] clung to the second stage of belief, which placed the seat of intellect and of emotions in the heart, arguing that the heart as the noblest organ must also be the seat of the noblest functions, but the superiority of the brain over the heart and the liver gradually came to be a part of popular belief as well as an axiom of anatomical science. Plato (Timaeus, § 69–71) shows the influence of this change in the compromise he proposes between the older and modern views. He assumes that man has two souls, one immortal and divine, which he places in the brain and to which he assigns the intellectual activity as the highest

[1] See Windisch, Ueber den Sitz der Seele, besonders bei den Indern und Griechen (Verhandl. d. Kgl. Sachs. Ges. d. Wiss., vol. xliii, pp. 155–191).

[2] See numerous examples in Audry, Recherches sur le Cœur et le Foie (Paris, 1858), pp. 1–30. I beg to call the attention of those interested in the history of medicine to this valuable (and almost forgotten) work, which contains a wealth of interesting material bearing on views held in antiquity—both popular and scientific or pseudo-scientific—as to the heart and the liver. Most of the references furnished by modern writers are to be found in Audry, besides many others that have been overlooked by his successors. Had I known of this monograph in an earlier state of my researches, it would have saved me much time.

[1] Cicero, De Divinatione, ii, § 24. See also Cicero, de Natura Deorum, i, § 26.

[2] Polyaenus Strategematon, iv, 20, ascribes this trick to a priest, Soudinos, whom he calls a "Chaldean" meaning probably "diviner" and who was in the service of King Attalus I, of Pergamos. Frontinus Strategematon, i, 15, tells the same story of Eumenes, the son of Attalus, and also (§ 11–14) of Alexander the Great.

[3] Fuchs, in Neuburger and Pagel, Handbuch der Geschichte der Medizin (Jena, 1902), i, p. 238.

[4] See De Partitione Animalium, ii, 10, and the other references in Windisch, l. c., pp. 171–174.

function; the other, mortal, which he places in the breast, with the seat of the lower emotions, as jealousy, anger, the passions, and appetites, below the diaphragm, and the seat of the higher emotions, as courage, above the diaphragm. The chief organ below the diaphragm is the liver; the chief organ above the diaphragm is the heart. The liver is thus degraded from the high and unique position it once occupied as the seat of the intellectual functions and of all emotions—the higher *and* the lower—to being the seat merely of the lowest emotions, and this position it still occupies in the popular usage of the present time, as is indicated in such phrases as "white-livered," in the sense of cowardly, "choleric" (from cholē = gall-bladder), for "passionate" and the like.

By the time that the view which gave to the brain the functions of soul-life had made its way into popular belief, the religious faith of Greece and Rome was too far advanced on the road to decay to permit of a further modification in the rite of divination. Greek philosophy had aroused a spirit of skepticism which gave to the current beliefs about the gods a blow from which the religion never recovered. In a skeptical age religion is apt to retire within its shell and to exhaust its energies in the effort to maintain what exists, rather than to branch out to new aspirations. Had the view which gave to the brain the position once occupied by the liver and subsequently by the heart come at a time when the prevailing religion was still in its full strength, we would have witnessed the addition of the brain to the organs of the sacrificial animal to be inspected with a view of divining the will and intentions of the gods. In phrenology, however, we have the expression —*outside* of the official cult—of this third stage of anatomical knowledge, and in so far as phrenology is still employed as a "quack" method of reading character, we may see in it a modified form of ancient divination. I am inclined also to see in chiromancy a link uniting the present to the ancient practice of divination through the liver of the sacrificial animal, since the reading of the lines of the hand appears to be merely the transfer to a more accessible part of the body, of the interpretation of the lines or markings on the liver, which, as we have seen, played so important a role in ancient hepatoscopy.[1]

Be this as it may, I trust to have demonstrated the thesis of the close alliance between divination and the early history of anatomy—complimentary to the bond existing between incantation rites and the beginnings of medicinal treatment of disease. In divination through the liver of the sacrificial animal we have a practical and plausible motive leading to the study of animal anatomy; and the study once begun would by the impetus of men's curiosity lead in the course of time to its divorce from the cult. We may, perhaps, go a step farther. Anatomy passes by a natural process to surgery, and it would appear that in Babylonia, at least, the practice of surgery was the first branch of the general subject of medicine to cut loose from the bondage to religion and to the religious cult. In the Hammurabi code the eleven paragraphs (§ 215–225)[1] dealing with medicinal regulations, all are concerned with the physician as surgeon, from which, therefore, we are justified in concluding that the name for the physician, *asû*, especially "healer," was originally applied to the surgeon. Since the code is conspicuous for the absence of regulations for the priesthood,[2] the surgeon is to be regarded as a layman and not as a priest.[3] Whether the same holds good for Egypt, where anatomy and surgery arise naturally in connection with the elaborate method of embalming the dead, is, I am told by Egyptologists, a question that cannot be definitely answered, though the indications are that while, as in Babylonia and Assyria, the treatment of disease was always retained in the hands of the priests and never entirely dissociated from the cult, such treatment could also be undertaken by laymen, and that surgery was entirely independent of religious rites, except, of course, in the case of circumcision, which as a distinctly religious act could only be performed by a priest.[4]

[1] Perhaps a trace of the connection between "liver" divination and chiromancy is to be seen in the designation "line of the liver" given to one of the markings on the hand

[1] See R. F. Harper's edition of "The Hammurabi Code" (Chicago, 1906), pp. 76–81.

[2] There are, to be sure, numerous regulations for the devotee, or "woman of the god," attached to the service of the temple, but she occupies a different plane from that of the priest.

[3] By a play upon the name *asû*, of which the Babylonians and Assyrians were so fond, the two parts of the word *a* and *su* were interpreted as "father (or "son") of knowledge." That the *asû* was, however originally a priest is shown by the fact that the two signs with which the word is written are set down as a synonym of *bārû*, literally the "seer" or "inspector," *i. e.*, of the sacrificial animal, which is one of the commonest terms for the "priest" as diviner.

[4] On circumcision and other forms of surgery among the Egyptians, see Prof. W. Max Müller, Egyptological Researches (Washington, 1906), pp. 60–62; On Egyptian Medicine, the "Harveian Oration" of Richard Caton (London, 1904); Reisner, the Hearst Medical Papyrus (University of California, 1905), Introduction, p. 1, and Erman, Life in Ancient Egypt, pp. 356–360 seq.

NÉLATON.

By Astley Paston Cooper Ashhurst, M.D.,
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Dupuytren was dead! The master surgeon of France, whose positive personality and despotic authority had so long overshadowed all other surgeons of his native land—this haughty and dignified chief, this pitiless operator, this man with actual contempt for human life, had passed on to that mysterious land from whose bourne no traveller returns. The eighth day of the month of February, in the year 1835, will ever be memorable in surgical annals. Dupuytren was dead! "The day of the funeral, the sky, since early morning, had been gloomily hidden by clouds of gray. Rain, fine and continuous, turning at times to snow, covered with ice the immense but silent throng which obstructed the *place Saint-Germain-l'Auxerrois* and the vast court of the house of death. Students' arms bore the precious burden even to the cemetery itself."

Dupuytren was dead! Life is short, and art is long. Who was to take up the work he had been forced to abandon at the early age of fifty-eight years? Who, among his contemporaries, his followers, his pupils, was equal to the task? For thirty years he, like the Turk, had borne "no brother near the throne." His career had been run so aloof from other men—his character had been so unexpansive—his habits so reserved—that there was no one who justly could be regarded in the light of his logical successor. Amussat, Jobert de Lamballe, and Leroy d'Étiolles, although well advanced in reputation at Dupuytren's death, were all of the younger generation. Boyer, who, in spite of his twenty years' seniority, may be regarded as a contemporary of Dupuytren, since he predeceased him by only two years, had, notwithstanding his many failings, this at least to his credit: that he had, unlike Dupuytren, trained up a worthy successor (Roux)—one who, by this prolonged apprenticeship, unfortunately lost in reputation what he gained in experience. Neither Breschet nor Sanson, who, during Dupuytren's last illness, had been his substitutes at the Hôtel-Dieu, was qualified to continue with equal éclat the career just terminated by death. The greatest name in French surgery between Dupuytren and Terrier—that of Nélaton—was then scarcely known, and although the post of surgeon to the Hôtel-Dieu was accorded to Roux, the mantle of the prophet fell on the shoulders of Nélaton. What there was to justify this encomium, in the personality, in the career, in the contemporary reputation of one who, alas! is known by name alone to many surgeons of today it is the purpose of this brief tribute to indicate.

A volunteer soldier in the armies of the Republic returned to Paris during the Consulate, and established himself as a *tapissier;* he there married, for his second wife, a young woman of intelligence and great strength of character, the

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daughter of a *maître-cordonnier*. Their second son, Auguste Nélaton, who was destined to make his family's humble name famous throughout the world, was born June 17, 1807. "One cannot but admire," says Guyon, "the laborious

evolution which, step by step, transforms an unknown name into one which is celebrated. It is one of the glories of a liberal profession, as well as of a free land, that a man's future is in his own keeping, and that even those who are born without other patrimony than that which hard work holds in store can, by their own efforts, acquire a distinguished position and an enviable reputation among their more favored contemporaries."

Nélaton's father, soon after the birth of his younger son, again joined the army (as *garde-magasin*); and although he kept his family with him for a time, he finally departed with the army on the desolate Russian campaign. For a year longer, letters and remittances came at intervals from the absent husband; but at length neither money nor news was received, and Mme. Nélaton and her children were added to that large company of widows and of orphans with which already Napoleon's quarrels had too much filled the world. The resourceful mother, who till then had existed in modest competency, now took in sewing, and by her adroitness soon acquired quite a *clientèle*. The elder son obtained a scholarship, and went to the College of Amiens, but the younger boy remained at home. Despairing at last of further word of her husband, Mme. Nélaton returned in 1821 to her family in Paris, determined that Auguste, who had now reached the age of fourteen years, should seriously commence his studies. These early years of close association with his mother were of utmost value in forming the boy's character. "He had early seen the force of kindly acts, the value of work, the power derived from constancy in one's affections and duties."

Passing through his school days, he entered the *College Bourbon*, with a name for conscientious and painstaking study. In the last year (1828) at college he was much attracted by a new tutor, who was himself a student of medicine. This young man was destined to have a great influence on the future of young Nélaton. The tutor's bedroom was often the repository for some anatomical preparation, carefully guarded from the eyes of the profane; but owing to the sympathy which soon sprang up between the tutor and his zealous pupil, Nélaton was sometimes allowed to contemplate these treasures. This new tutor—the young medical enthusiast—was no other than Achille-Pierre Requin, who later became the colleague of his former pupil in the Faculty of Medicine of Paris.

It was owing to the conversations, the counsels, and the example of Requin that Nélaton was persuaded to enter the medical profession. On leaving college, in 1828, he was accordingly entered as student of medicine of the Faculty of Paris. His studious habits were continued. Anatomy had special attractions for him. Often, we are told, in the old amphitheatre of La Pitié he would prolong his dissections until darkness overtook him at his work. His attention to his studies was unremitting. He was laying the foundations broad and deep. It is narrated of him, possibly with some exaggeration, that he so grudged the hours allotted to sleep that he used to lie at night on a narrow board supported between two chairs; "when he fell asleep through sheer fatigue, he would fall with the board, pick himself up, and set to work again."

Among his fellow students and contemporaries were Diday, Denonvilliers, the two Bérards, Cazeaux, Tessier, etc.

In 1830, while still an undergraduate, he served as *externe* under Dupuytren, at the Hôtel-Dieu. The great ambition of all the students then was to become Dupuytren's *interne*. This was never to be Nélaton's privilege. Disappointed time and again when the names of the successful candidates were announced, Nélaton never ceased to haunt the corridors of the Hôtel-Dieu. He followed the great master's clinical teaching, hung upon his words, and observed, we can scarcely doubt with jealous eyes, the duties performed in the wards by his more favored competitors. In the historic corridors of this ancient hospital, long since replaced by other buildings, the entrance of Nélaton always created a stir among the future great men who were habitués of the place. He gained at once the sympathy of all.

In 1834 Nélaton received the appointment of *interne* at the *Hôpital des Enfants-Malades*. Far from despising an excellent service merely because it was not the most coveted, he soon proved to his chief, Baffos, that he was worthy of all confidence. As a consequence, Baffos, who was convinced that those things are learned best which are learned by one's own experience, and who consequently made it a rule to let his assistant do with his own hands as much practical work as he could conscientiously turn over to him, found in Nélaton an assistant so much to his liking, and found him doing such excellent work, that it is doubtful whether Nélaton did not learn more in this service than if he had received instead the appointment under Dupuytren. Determined here, as always, to make the most of his opportunities, Nélaton collected material for his inaugural thesis, "Sur l'affection tuberculeuse des os" (1836). This work was a revelation. Founded on material which in no way differed from that which had been accessible to others for years before, but which no one had thought worthy of such attentive study, Nélaton by this essay once and for all created a definite place in surgical treatises for tuberculous disease of the bones.

At the end of this term of service at the *Hôpital des Enfants-Malades*, Nélaton was still undecided whether to adopt surgery or medicine as his profession. Baffos bluntly told him: "You're a fool! Make surgery your life work." The advice was accepted; and finally, the assiduous applicant for the post of *interne* under Dupuytren at last had his desire gratified. In the year 1835, when twenty-seven years of

age, Nélaton's name was at last entered as Dupuytren's interne. But the revered chief was no longer there; overtaken by his last illness before Nélaton's term commenced, his career was stopped by death, February 8, 1835. But the grand memory which the pupil retained of the dead surgeon had the most decisive influence on his career, and Sappey, who knew Nélaton more intimately than most men, wrote that Nélaton had, as it were, "grandi à l'ombre et dans le culte de la mémoire de Dupuytren."

Having received his degree in 1836, Nélaton became, in 1838, a candidate for *Professeur Agrégé* in the Faculty of Medicine. He had none of the usual recommendations for obtaining this election. He had no influential backing; he was not a "son of the Faculty;" he had never been "aide" in anatomy, nor prosector; and those who had served in these posts were always regarded with most favor for election to chairs in the Faculty. Candidates for positions in the Faculty were in those days accorded a public hearing, and at this, his first *Concours*, Nélaton felt the extreme weakness of his candidacy. But those who had watched his career hitherto did not regard him as an unworthy antagonist; so that when he presented himself, with his diffident manner, and spoke, not as orator, but as student, he himself was the only one surprised at the result of the election which gained him the desired position. This appointment was followed, Diday tells us, by a period of continuous, indefatigable labor, which bore its fruits later for Nélaton, but of which the immediate result was quite characteristic. He was productive, he was copiously productive; but others received the honor of his labor. Every day a new author, a candidate just beginning to make progress, or even some professor himself, from whom the editor had extracted the promise of an article for the *Dictionnaire*, came to find Nélaton. He was asked for advice, and he presented a complete *mémoire*. Sometimes this generosity was carried to an extreme; in 1844, for example, during a "*concours d'aggrégation*," all the candidates wished his advice for their theses; and, as he was unwilling to refuse any, he found himself so overwhelmed that he finally had to establish himself at the very post of combat, and finished by spending the entire night at the printer's, correcting the last proofs.

Being appointed, in 1839, Surgeon to the Hospitals, he determined to publish an extensive work on surgical pathology (*Elements de Pathologie Chirurgical*, 5 vols., Paris, 1844 to 1859). His old friend and tutor, Requin, was to write the medical portions of this extensive work. Nélaton was unable to complete more than the first two volumes unassisted, and was forced to enlist the aid of Jamain as collaborator in the production of the third, fourth, and fifth volumes. Nélaton often repeated that a surgeon wrote books before he knew how it should be done, but that he had no longer the opportunity to write when he had learned by experience that which a good classical work should contain.

In 1850 Nélaton became a candidate for the chair of "Médecine Operatoire" in the Faculty of Medicine. Malgaigne was elected. In 1851 the contest was renewed for the chair of "Chirurgie Clinicale." His opponents included not only Lenoir, Robert, and Michon, who had participated in the contest the previous year, but also one of the most distinguished professors of Montpellier. This *Concours* of 1851 was one of the last in which the old custom was continued of having a public contest of the various candidates. Many might have thought that Nélaton's modesty, his retiring disposition, and his lack of an imposing list of monographs published over his own name would have been against him. But neither the public nor the jury were deceived. "That man—one knows that he knows," said a good judge; and Nélaton's election followed. Possibly, is is said, another motive lay behind the election. "Oh! so far as *he* is concerned," murmured to himself one of the Faculty, "he can be elected in all safety; *he* will never have much of a private practice"; and this was not said so low that it was not well heard on all sides of the speaker. But this prognostication was false, for Nélaton had later an immense success in private practice. "But Nélaton was always the same unassuming, modest man, and obtained celebrity while studiously avoiding renown."

Nélaton was now forty-four years of age. As Professor of Clinical Surgery he continued with increasing favor the brilliant courses of clinical lectures which had already begun to draw students from all parts of the civilized world. His teaching was, above all, lucid, logical, and direct. He spoke slowly, without eloquence, but to the point. His propositions were built one on the other, so closely that one had but to listen to understand; and his hearers so soon perceived that everything uttered would be perfectly intelligible, that their attention never for an instant wavered. In the presence of rare or hitherto unknown lesions his students were astonished at his unerring power of reaching a correct diagnosis. It was, however, no mere intuition on his part; it was simply the application of the same principles of the science of diagnosis which in ordinary cases lead to a similarly correct result. He was unwilling to admit that a real diagnosis could be made on sight. By some lucky chance such a guess might happen to be correct, but to his mind even a correct guess was not a diagnosis. His conclusions were the result of systematic observation, correction, correlation, and meditation. He studied his cases carefully and repeatedly. It may at first have seemed tedious to his internes, the long rounds and the conscientious inquiry into the history of the disease, with the physical examination which he made in person; but they soon perceived that here was a past master in the art of teaching and the cure

of disease, who was still studying his cases as if some error might creep in unawares to mar the successful result. It was no rare thing for him to return again to the hospital in the afternoon, to examine anew the patient who was to form the subject of the morrow's lecture; thus satisfying himself by repeated evidence of some surgical fact which had an important bearing on the diagnosis or treatment of the affection in question. It was this absolute familiarity with his cases, this intimacy with the clinical course of the disease, which rendered his teaching so authoritative and clear, and his therapeusis so successful and gratifying.

He was above all things a practical man; he was not a lecturer like Velpeau—erudite, versatile in all departments of surgery and obstetrics, and fond of generalization. Calm and dispassionate, with a full mind and a ready hand, Nélaton studiously shunned the least appearance of brilliancy. In manner he was pleasant, while reserved; far more a man of the world than the brusque and comparatively rustic Velpeau. Velpeau loved to amaze by his learning, entrance by his eloquence, and, in general, preferred the form of his teaching to the matter. Nélaton desired above all things to be considered an exponent of an art which was beneficent and humane. He wished surgery to be gentle; and he was happy to think that patients who forgot in after life the pangs surgery had made them endure retained an affectionate memory of the surgeon.

He never complained of enemies, although doubtless he had some; but he never gave them the proud satisfaction of being talked about. As he was ignorant of how to triumph, so he did not know how to complain. This happy moderation of sentiments pervaded all his acts. "I don't know how Nélaton manages it," Velpeau used to say. "He never seems to be in a hurry."

As an operator he had the true "sang-froid"—that certainty of procedure founded on definite plans to accomplish given ends, obtained by his exact anatomical knowledge and his acquaintance with what might reasonably be accomplished by surgical measures. He never would operate at his first visit, always leaving time for reflection. He would not attempt an operation as a mere experiment. He was not original, but he had the great merit of being able to amend, correct, and complete anterior surgical conceptions. When a novel operative procedure was to be employed, or one with which, although previously employed by others, he had no personal familiarity, he would resort again to the dissecting room, and there work out the problem as it seemed to him to be most satisfactorily solved. Frequently, by some little modification of the previous technique, by some slight inversion in the order of the steps of the operation, or some other trifling change, he would convert a procedure of hitherto doubtful expediency into an operation of wide application and lasting utility. "He was often regarded by his pupils as *fortunate* in his operations; but when these pupils had themselves become practitioners they easily recognized the fact that success in surgery oftenest waits on those who neglect no precaution and abandon nothing to chance."

Nélaton, moreover, had the courage of his convictions. He advocated gastrostomy for impermeable stricture of the œsophagus, although at the time the operation had been done only twice (by Sédillot, of Strasbourg), and although both patients had died. He advocated and practised tracheotomy even *in articulo mortis* from croup; and this in spite of the fact that, save for one initial success, he recorded twenty-five consecutive tracheotomies with a uniformly fatal result. He believed operation was the proper thing, and he was not one to be terrified by figures into letting a patient die in peace when surgery offered the only hope of recovery. The operation of ovariotomy, although widely practised in America by McDowell and the Atlees, and also in England, was considered in France mere butchery, not worthy the name of surgery. Nélaton was not appalled by the clamor of his more timid countrymen. In 1861, at the age of fifty-four years, he made a trip to England, to see for himself this dreadful operation and to convince his own mind as to its legitimacy. He saw and believed. He returned to Paris and gave his countenance and support to another surgeon (Demarquay), to whom first an opportunity came of employing the operation. And although the patient died, Nélaton upheld the practice, and declared that he would himself employ this operation at the first opportunity.

As stated by his biographer, Béclard, Nélaton poured forth from generous hands, and without counting, a horde of ideas and useful principles which even at this late day circulate in public, and seem to belong to no one in particular; so much so, indeed, that it can truthfully be said Nélaton's surgical work exists nowhere and yet is everywhere present. Among the operations indelibly associated with his name, and one which is still occasionally practised with success, is that of enterotomy for acute intestinal obstruction (1840). Although employed before Nélaton's time, it was he who urged suture of the intestine to the parietal peritoneum before opening the gut, so as to prevent contamination of the general peritoneal cavity. He improved on the operation for artificial anus by first dissecting up the edges of the fæcal fistula and uniting them, and then by sliding over this deep plane of tissues a superficial plane composed of a bridge of skin attached at its two ends. By utilizing the periosteum in his flaps for rhinoplasty he made the new nose firmer and more enduring in outline. He insisted on the necessity of ligating in the wound both ends of the divided artery, instead of relying upon ligature of the main trunk above the wound, as practised by most French surgeons at that time in imitation of Anel, although Guthrie had long since established in English surgery the principle for which Nélaton contended.

In a case of pulsating exophthalmos, Nélaton correctly diagnosticated the presence of an intracerebral arteriovenous aneurysm; he ligated the internal carotid artery; and although deprived of the joy of seeing his patient permanently recover, had at least the melancholy satisfaction of having the correctness of his diagnosis verified by the autopsy. He operated with success for ununited fracture of the humerus, by resection and fixation of the fragments. Nélaton's dislocation is the name given to luxation of the ankle upward between the bones of the leg. The principle of adduction of the hand, in fractures of the lower end of the radius, still in constant employment, was the idea embodied in his pistol-shaped splint. The soft rubber catheter in universal use was introduced by him. His name will ever be associated with the applied anatomy of the hip-joint.

Brought up in hospitals where he was surrounded by those dreadful complications of wounds, whose attenuated forms, as Béclard expresses it, are termed angeioleucitis, erysipelas, or phlegmon, Nélaton early adopted alcohol as a surgical dressing. The former custom had been to stuff the wound with charpie, so as to promote healthy suppuration. He inveighed against the fashion then creeping into surgery of hermetically sealing all wounds with sutures, with the idea that by preventing the contact of the air all fear of suppuration would be abolished; but he did not possess the originality which enabled Chassaignac to introduce (1859) the rubber drainage tube, and thus combine the advantages of the two methods.

On August 29, 1862, the illustrious Garibaldi, the idol of his compatriots and the most famous soldier in Europe, while at the head of his troops at the battle of Agramonte, received at the same time three balls from among those in the first discharge fired by the regular Italian troops. The first merely bruised his left knee; the second caused a slight wound of his right buttock; but the third lodged in his right leg, a little above and in front of the internal malleolus. The surgeon on the field of battle, Albanese, thinking there was evidence that the ball had penetrated nearly to the skin on the back of the ankle, made a counterincision at this point, but could not find the bullet. Transported by boat, Garibaldi was brought to the fort of Varignano, at Spezzia, on the evening of September 2. Two days later, in the presence of Albanese, Rizzoli, Zannetti, Bazile, and others, Prof. Porta, of Pavia, explored the wound. The consultants came to the conclusion that the ball was no longer in the wound. Bazile, however, was not convinced. Nélaton, called in consultation, arrived at Spezzia on October 28. Garibaldi had now been confined to his bed for two months. Scarcely had Nélaton begun to examine the wound than his practised hand and attentive ear detected the bullet. Pirogoff, who, with another Russian surgeon, arrived three days later, was of the same opinion. It remained for Nélaton to convince his Italian confrères. He returned to Paris, reflecting on the methods he could use to demonstrate the presence of the ball to others. At the suggestion of a friend, that some small body should be introduced into the wound which would retain an impression of the bullet, Nélaton had constructed his well-known porcelain-tipped sound. Sending this to the surgeons in charge of Garibaldi, he had the satisfaction to learn of the successful result of the test made by Zannetti, who had failed to demonstrate the bullet's presence by more complicated experiments made with a galvanic battery.

The presence of the ball being thus demonstrated, Zannetti proceeded with the greatest facility to its extraction, and Garibaldi was soon restored to health.

The renown which came to Nélaton as a result of this episode resulted in making his name a household word throughout the civilized world. Although his authority in France was previously acknowledged, his preëminence now became incontestable. He was astonished at his own success, and mortified and embarrassed by the immense income which he made in the practice of his profession.

It is said to have amounted to 500,000 francs a year ($100,000).

The succeeding years were marked by elections and appointments which testified to the esteem in which he was held by his colleagues, by the French people, and by his sovereign. At the death of Jobert de Lambelle, in 1867, Nélaton had the honor of succeeding him both in the Academy of Sciences and as Surgeon to the Emperor. In 1868 he was made Grand Officer of the Legion of Honor and Senator of France. A year earlier, although only sixty years of age, he had resigned his professorial chair because of failing eyesight and uncertain health.

It is a tradition from the time of Celsus that a surgeon should be young; and there is no profession whose tireless activities and ceaseless lack of repose so soon consume a man's youth as does that of surgery. Perhaps, too, there is no more difficult thing for a surgeon to do than to grow old gracefully—to feel his clearness of vision, his steadiness of hand, his pitilessness in operating, each and all of them day by day retained with an ever-increasing exercise of will, and with an ever greater effort of self-control; this must be torture to any surgeon. So those who begin to feel the need for repose, and who have intimations that their outward frame decays, do well to withdraw from active practice ere yet their eyes are dimmed or their natural force abated.

Yet Nélaton, in spite of his efforts to retire, found no repose. The stirring events of the Revolution of 1870 were at hand; events came headlong one after the other; the days of the siege arrived. "Like all of us," writes Béclard, "Nélaton wished to do his duty in the ambulances; this last effort completely broke his constitution. The disease of the heart,

from which he had for some time suffered, now made rapid progress. His walk became more labored; an expression of fatigue and sadness replaced on his benevolent countenance the smile which had habitually lightened it. His circulation became daily more impaired, and day by day he seemed to be leaving us." It was mere force of will power that kept him going. Finally, he was persuaded by his family and friends to leave Paris. But neither Italy, nor the sea, nor the pure air of the country fields could stay the hand of Death, and he returned to Paris barely in time to die. His death occurred on September 21, 1873.

"Tant qu'il vécut, notre ami s'appliqua, on le sait, à ne laisser faire autour de son nom que le moindre bruit possible; et il n'a pas dependu de lui que ce silence ne fut continué autour de sa tombe."

I began this sketch with a brief reference to the death of Dupuytren. Self-contained, studied to the point of self-consciousness in all his actions, impenetrable, Dupuytren had more high lights in his character than Nélaton, but also more shadows. Nélaton was simple, open, accessible to all; his only fault was his humility. He would not create a "school." He has left us little to read. There is a danger that his personality will be forgotten.

At his funeral there was none of the pomp and grandeur that accompanied the obsequies of Dupuytren. His body was borne to its last resting place on a gentle day in autumn. "No discourse was pronounced over his tomb. He had wished for silence; his wish was piously respected. On the funeral car, around which his loved ones and intimates pressed, there was nothing to recall the great dignitary of the State, the Academician, or the Professor. As we followed his modest bier, enshrouded in flowers, the memory of the eminent surgeon associated itself involuntarily in our thought with that of one of the greatest naturalists France has known. It was not in the midst of the pleasures of fortune, but in a bare chamber and with a hand chilled by misery, that Michel Adanson requested that the sole decoration of his bed of death should be a garland of flowers taken from each of the vegetable families which he had established—a passing image of the more durable monument which he had erected for himself."

Homines semper postrema meminere.
Tacitus.

A NEW INSTRUMENT FOR MEASURING MARKED DIFFERENCES IN EXPANSION ON THE TWO SIDES OF THE CHEST.

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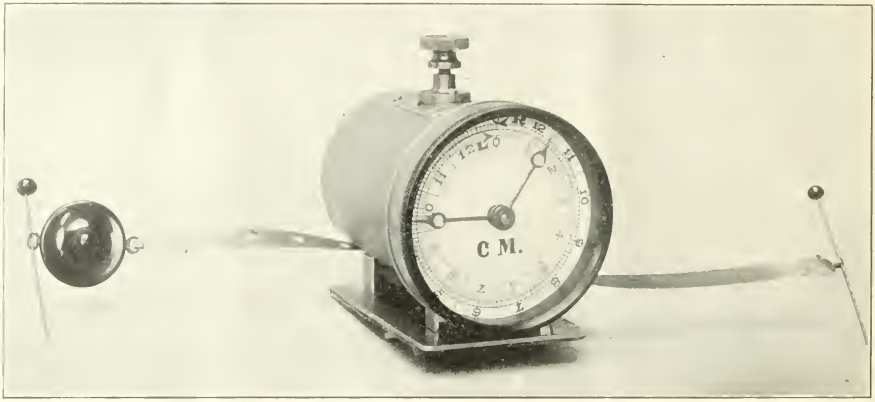
The instrument shown in the accompanying illustration was designed with the hope of its being of some diagnostic value in determining differences in the expansion of the two sides of the chest. This hope, however, had to be abandoned, as it proved to be of not sufficiently delicate accuracy, and its use is limited to that indicated in the title, the demonstration of marked differences of expansion on the two sides of the chest.

The instrument consists of a metal cylinder, on the top of which is a dial with centimeters marked in both directions from the zero point. Running from either side of the metal cylinder is a steel tape (*A B*), to the end of which a button (*C*) is attached. These two tapes work upon cylinders, the movements of which are independent of each other. Each of these cylinders is controlled by a spring, and is connected with the hands registering on the dial in such a way that the tapes may be withdrawn and allowed to return at will, the hands meantime remaining perfectly stationary. As soon, however, as the button *D* is pressed downward, the hands and cylinders are connected, so that movements of the tapf are registered in centimeters on the dial. The advantage of this arrangement will be seen in the manipulation of the instrument.

To use the instrument, the disk *E* is placed upon the sternum, a little below Ludwig's angle; the tapes are drawn horizontally about the chest and joined to the button *C*, which is placed directly upon the spinal column. With the instrument in this position, the patient inspires and expires at will without the respiratory movements having any influence upon the hands, both of which are resting at the zero point. At the beginning of any chosen inspiratory act, with usually the coincident request to the patient for a deep inspiratory effort, the button *D* is depressed, and the two hands move in accordance with the increase in circumference of the respective sides of the chest, the expansion of the right side registering on the outer line *R;* the left, on the inner

line *L*. The two features which are apparently most potent in preventing the registration of small differences in expansion are the various degrees of compressibility of the soft tissues of the chest and the friction that at times exists between the skin surface and the steel tapes. These two conditions make possible the registration of only such degrees of difference as could be appreciated, though not so graphically, without the use of an instrument.



CHRONIC CYSTIC MASTITIS.[1]

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(From the Laboratory of Surgical Pathology, University of Pennsylvania.)

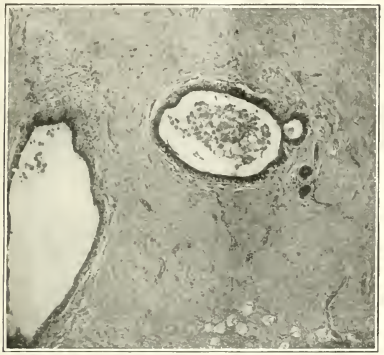
The attention of surgeons was first directed toward this disease particularly by the writings of König, Reclus, and Schimmelbush. More recently, however, additional information and interest have been derived from the studies of Greenough and Hartley and Warren. While new data of much importance, from a pathological standpoint, cannot be added to the results obtained by the last-named writers, the author deems the subject one of such importance and the disease so common (13 per cent. of all breast diseases) that he ventures to present it before this society.

It is necessary for a complete appreciation of the pathology of the disease to understand the changes which occur in a normal breast at the time it undergoes involution, for the two processes seem to be intimately connected. As a part, then, of the cessation of the sexual functions at this time, we find the secreting elements of the breast undergoing involution. This is accompanied by an extensive overgrowth of interlobular connective tissue, dense in character, and containing few cells. The interlobular tissue hypertrophies, and by its contraction causes atrophy of the glandular and fatty tissues, while at the same time the characteristic periacinous tissue of the breast undergoes hyaline degeneration and disappears. Up to this stage the process can be regarded as a physiological one, and it requires but slight impetus in such an organ to cause abnormalities which may bring about a grave pathological lesion. Warren has given the name "abnormal involution" to the series of changes which predispose to the disease commonly termed "chronic cystic mastitis," and this deviation from the normal has been well studied by Greenough and Hartley (*Journal of Medical Research*, June, 1903). They believe that the increase of connective tissue which occurs in a breast undergoing abnormal involution and the cystic changes which result in the ducts and acini from obstruction by this thickened tissue are not as important as the effect this process has

[1] Read at the meeting of the Medical Society of the State of Pennsylvania, held at Reading, September 23–26, 1907.

on the breast epithelium. The latter, by reason of the cysts formed, becomes even more unstable than it is normally, and tends to undergo extensive proliferation. In many cases this proliferation does not extend beyond the limits of what may be considered a benign process, but in others, about 12 to 16 per cent. of the cases, the epithelial hyperplasia is of such a degree that a malignant degeneration can be diagnosticated.

cystic; (2) the proliferative group, in which the epithelium of the cysts is hyperplastic (Figs. 1 and 2). Histologically, the proliferative class is further subdivided into (*a*) those instances in which epithelial proliferation occurs in the acini; (*b*) those showing the presence of distinct papillæ in the cysts; (*c*) the formation of adenomatous areas. From cases in which adenomatous proliferation has occurred we find the tendency toward malignant degeneration most likely,



FIGS. 1 and 2.—Photomicrographs showing epithelial desquamation, hyperplasia, and cystic dilatation.

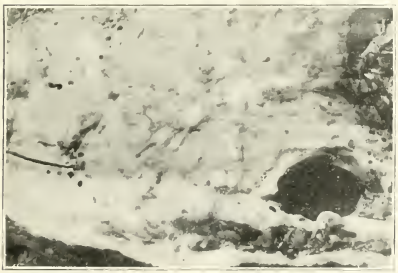


FIG. 3.—Cyst surrounded by dense white tissue, resembling carcinoma.

The proliferation of epithelium is considered by Greenough and Hartley as a reactionary hyperplasia placed under abnormal conditions. Some writers have described the disease as a distinct tumor formation, and by others it has been looked upon as of inflammatory nature; the latter views are not being borne out, however, by pathological examination.

Two types of the disease, occurring with equal frequency, are described: (1) Those in which the changes are distinctly

and, as would naturally be expected, the carcinoma is usually of a glandular type. As the characteristics of these groups are recognizable only on microscopic examination, and as the cases symptomatically are identical with other forms of the disease, a further consideration of the histological differences is not considered necessary.

Even when the epithelial proliferation has become sufficiently great to be classed as carcinomatous on histological examination, the symptoms are not sufficiently marked in early cases to make this change apparent. It can readily be appreciated, therefore, that operative interference and careful microscopic study of the breast tissue removed are always indicated in chronic cystic mastitis. In the cases which have been operated upon at the University Hospital the malignant nature of the disease in one instance only could with any degree of accuracy be determined previous to operation.

The gross appearance of the diseased tissue is, as a rule, characteristic, consisting of a dense, white mass of fibrous tissue containing cysts of varying size. In the majority of cases the greater part of the breast is involved, although occasionally the process is circumscribed. The induration in some instances is not unlike carcinoma, and in one of the cases of this series the diagnosis of a malignant growth was

made from the gross appearance, but was not confirmed by the most thorough histological examination (Fig. 3). The cysts are often under considerable tension; they vary in size from a pinpoint to an egg; their contents are, as a rule, clear, although discoloration of the fluid is not uncommon.

The disease occurs usually in women who are approaching the menopause, although it is not uncommon in young women, the one in Case XII being only twenty years of age. As a rule, the indurated area is discovered by accident, and if observed from this period, its growth is slow. At times, however, there is an appreciable increase in the size of the cysts, which, if not accompanied by any discharge from the nipple, would lead one to suppose that the process had become malignant. The indurated area, when not diffuse, is situated most commonly in the upper outer quadrant of the breast.

The opposite breast should be carefully examined, for in a small proportion of cases it is similarly involved. The mass often causes pain, and is sometimes decidedly tender on palpation. The skin is never adherent, and the nipple is sometimes inverted, according to Warren, but was not thus affected in any of the cases to be reported. The axillary lymph nodes are occasionally found enlarged, the hardness is not as marked as is the case in secondary carcinoma of the nodes, and the enlargement is not progressive in nature.

Chronic cystic mastitis is mistaken most commonly for carcinoma, puerperal mastitis of infectious origin, adenofibromatous growths, and the various forms of retention cysts. The diagnosis, in many cases, is practically impossible, and in any event an immediate diagnosis can be made microscopically. It is the custom at the University Hospital to make frozen sections in all breast cases in which the diagnosis is uncertain. This measure is one calculated to save the patient much discomfort, for, if the diagnosis of malignancy can be made while the patient is still under the influence of an anesthetic, the danger of a second operation is obviated, and a more radical operation can immediately be undertaken. The question as to the advisability of a radical removal of the breast in cases which present the earliest forms of a carcinomatous change engrafted on a chronic cystic mastitis is a most important one. In one of the cases reported, the ordinary plastic removal of glandular tissue was performed and its malignant nature discovered at a later microscopic examination. There has not been any recurrence after six months, and a radical operation was not performed. It seems, however, a decided risk, and according to the writer's opinion amputation would be justifiable in view of our present knowledge of breast cancer, its dissemination, and the nature of the operative results obtained by the modern operative methods. If a radical operation is not determined upon, the patient should be under close observation to detect any evidence of an early recurrence.

Realizing the dangers of malignancy in so large a proportion of these cases, removal of the indurated areas is certainly indicated. Amputation of the breast was performed years ago, although such a disfiguring operation can be avoided by following Warren's technique (*Jour. Amer. Med. Assoc.*, July 15, 1905). An incision is made at the base of the breast extending to the inner border of the axilla, in order to cut the lymph vessels running from the breast to the axilla. The breast is freed from the pectoral muscle and reflected upward in order to expose its posterior surface. Cysts or indurations can then be removed by excising V-shaped sections, and the breast explored by radiating incisions in any direction. The openings are closed with catgut, and, if a large portion of the gland has been removed, a purse-string suture will bring the remaining tissue together, so that when the skin edges are once more in apposition there is a distinct protrusion of the nipple and the organ retains its characteristic shape. The operation is almost invariably followed by cure, the cysts rarely recurring, and the cosmetic result is most gratifying.

For permission to report and study the following cases, the author wishes to express his thanks to those surgeons in whose services they occurred.

Case I.—(Dr. Frazier.) T. Y., aged forty-seven years, is married; has no children. One year ago the right breast was amputated for carcinoma; no recurrence. Three days ago a lump in left breast, situated in upper outer quadrant, and about the size of a walnut, was noticed. The tumor was hard, not adherent to skin, movable on the underlying tissues, and not painful. Operation: amputation because of malignancy of tumor removed from the opposite breast. The breast contained a number of smaller cysts besides the one noted, and was involved throughout its entire extent. Result: cure, three months elapsing from time of operation. Pathological diagnosis: chronic cystic mastitis.

Case II.—(Dr. Martin.) A. H., aged twenty-two years, married, has one child. Tumor was in upper quadrant of left breast, two months' duration, size of an egg, painful; axillary nodes normal. Operation: excision of affected tissue. Result: no recurrence, after ten months. Pathological diagnosis: chronic cystic mastitis.

Case III.—(Dr. Frazier.) L. L., aged thirty-seven years, married, has three children. Lump was in upper outer quadrant, of three years' duration, with slight pain. Examination revealed a number of small nodules in breast, the entire mass being the size of a lemon; not adherent, axillary nodes not involved. Operation: plastic resection. Result: cure after twelve months. Pathological diagnosis: chronic cystic mastitis.

Case IV. (Dr. Frazier.) M. B., aged forty years, married, has one child. Tumor was size of an egg, in upper outer

portion of breast, of five weeks' duration, with no adhesions between growth and surrounding parts; axillary nodes and skin not involved. Operation: plastic resection of growth. One month later a number of cysts were palpable in the breast, and the axillary nodes were enlarged. Because of the danger of malignancy, although the diagnosis of chronic cystic mastitis was made at the first operation, it was thought advisable to remove the entire breast and the enlarged nodes. The latter on microscopic examination were the seat of a chronic inflammatory process; the breast, free from any malignant change, showed an extensive involvement. Result: cure, after eight months. Pathological diagnosis: chronic cystic mastitis.

Case V.—(Dr. White.) M. W., aged thirty years, single, noticed a lump in left breast eight months before admission. On examination, tumor size of hen's egg was found in upper inner quadrant of breast, freely movable, skin not adherent, painful, glands not involved. Operation: excision of cyst and surrounding tissue. Result: cure, after two years. Pathological diagnosis: chronic cystic mastitis.

Case VI.—(Dr. Martin.) L. P., aged forty-five years, married. Condition was noted two weeks before admission because of pain which was first experienced at that time. Tumor size of walnut was situated in upper quadrant, not adherent, with a few nodes in axilla palpable. Operation: amputation. Result: cure, after sixteen months. Pathological diagnosis: chronic cystic mastitis and adenocarcinoma.

Case VII.—(Dr. Frazier.) S. V., aged forty-five years, married, has two children. Trouble followed a fall three years ago, some months after which she noticed tumor in breast. Examination showed a mass in lower inner quadrant of breast; no adherence to surrounding parts; frequently causing considerable pain; axillary glands not involved. Operation: amputation. Result: cure, after three years. Pathological diagnosis: chronic cystic mastitis.

Case VIII.—(Dr. Frazier.) J. S., aged thirty-seven years, married, has no children. Tumor in lower outer quadrant of breast of three months' duration, was painless, freely movable, and the size of a small orange. Axillary nodes were not involved. Operation: plastic resection of mass. Result: cure, after thirty months. Pathological diagnosis: chronic cystic mastitis.

Case IX.—(Dr. Martin.) S. R., aged forty-five years, married, has one child. Five years ago the patient felt a small mass in outer lower quadrant of breast. She did not experience any symptoms until a few weeks before operation; at this time there was considerable pain, and the mass, the size of a walnut, increased in size; skin was adherent and tumor not attached to deeper structures. Operation: excision of breast; removal of axillary nodes, which were found enlarged. Result: cure, after thirteen months. Pathological diagnosis: chronic cystic mastitis and adenocarcinoma.

Case X.—(Dr. Carnett.) Patient aged forty-three years, single, has had several operations on right breast, two cysts being removed, the tissue, however, not being examined microscopically; for several months has suffered with pain in left breast, which on examination contained three distinct cysts, one to the inner side of the nipple, and one each in the upper and lower outer quadrants of the breast. The tumors were freely movable, the lymph nodes not enlarged; the skin not involved. Operation: plastic resection, all glandular tissue being removed because of the extensive involvement. Result: cure, three months. Pathological diagnosis: usual lesions of chronic cystic mastitis, and early malignant degeneration in form of adenocarcinoma.

Case XI.—(Dr. White.) I. B., aged forty-nine years, married, has two children. Lumps were first observed in right breast five years ago, the left being involved several years later. There was no pain nor tenderness; the axillary lymph nodes were not involved. Operation: because of rapid increase in size of indurated areas, plastic resection was performed. Result: cure, two months. Pathological diagnosis: chronic cystic mastitis.

Case XII.—(Dr. Kennedy.) M. A., aged twenty years, single, had lump in outer quadrant of breast for at least five months, producing decided pain and tenderness, without other symptoms; on palpation it was found to be the size of a hen's egg. Excision of indurated tissue was followed by cure, two months elapsing. Pathological diagnosis: chronic cystic mastitis.

CONTRIBUTIONS TO THE ANATOMY OF THE PARATHYROID BODIES, WITH ESPECIAL REFERENCE TO THE SURGICAL ASPECTS.

By Nate Ginsburg, M.D.,

Assistant Demonstrator of Anatomy, University of Pennsylvania; Clinical Assistant Surgeon to the Philadelphia Polyclinic and College for Graduates in Medicine.

(From the Department of Anatomy, University of Pennsylvania.)

The existence and importance of the glandulæ parathyroidæ have received much attention since the clinical significance of these structures was first suggested by Gley in 1891. While numerous contributions to the anatomy, physiology, and pathology of these bodies have appeared from time to time, the development of tetany after their removal during operation upon the thyroid gland in the clinical and experimental laboratories has furnished us with the strongest proof of their functional importance.

Sandström, Gley, Kohn, Verebeley, Welsh, Rogers and Ferguson, Poole, Halsted and Evans have all studied the human parathyroids, and contributed to their anatomy, both gross and microscopic.

Although Sandström, in 1880, eleven years before Gley's discovery, first recognized and accurately described the gross anatomy and histology of the human parathyroids, the excellent paper of Welsh (1898) is probably the most complete contribution dealing with the anatomy of these little bodies. This author described their position, based upon a large number of dissections, and gave an accurate description of the histology of these structures for purposes of differentiation from lymph nodes and remnants of thymus and thyroid tissue in close proximity to the parathyroid glandules. A review of the literature covering the previous studies on the parathyroids is embodied in Welsh's paper.

Position. Based upon careful examinations of the thyroid gland in a large number of specimens in the Anatomical Laboratory of the University of Pennsylvania, the parathyroid bodies may be said to be invariably present. Failure to find them does not necessarily indicate their absence, since their apparent absence may be due to an unusually thick collar of surrounding fat; the bodies being concealed by being embedded on the posterior surface of the lobe of the thyroid gland, thus appearing as part of the gland; or again, owing to their low position in the neck, they may lie beyond the scrutiny of the surgeon or the dissector, who limits the field of investigation too closely to the immediate proximity of the thyroid gland.

The number of parathyroid glandules is variable. Four, a superior pair and an inferior pair on each side, is conceded to be the most constant number and arrangement. Verebeley found four parathyroids 108 times in 138 autopsies. It is not unusual to find more than four parathyroids, as many as five and six having been described, but only a very careful and minute dissection of the thyroid gland and adjacent structures, supplemented by microscopic examination, can determine precisely the exact number of these bodies present.

The position of the parathyroids is a matter of great anatomical and surgical importance. While it is true that in a very fair proportion of cases these structures have a somewhat constant site, their position is variable in a sufficiently large number of cases to justify the statement that they may be found on almost any aspect of the thyroid gland.

In the largest percentage of the subjects examined the parathyroids were found, as Halsted expresses it, "in line with the channel of anastomosis," between the inferior and superior thyroid arteries. Their proximity to the inferior thyroid artery is more constant than to the superior thyroid artery. The little bodies were found lying either on the posterior surface of the lateral lobe of the gland in a separate sheath or within a split of the thyroid sheath, or partially embedded in the substance of the gland, but visible upon close examination. Parathyroids above and behind the upper pole of the thyroid gland were not unusual.

Next to the most constant site, *i. e.*, at the middle of the posterior surface of the thyroid gland, opposite the cricoid cartilage, the region of the lower pole of the thyroid was found to be the most common situation. In this region the parathyroid bodies were found with less difficulty, and here attained their largest size.

Vascular Supply. My experience has been similar to that of Welsh, Halsted and Evans, who found the little bodies supplied with a separate vessel, the parathyroid artery, a branch of the inferior thyroid. The superior thyroid artery may, however, give off a parathyroid branch especially in those cases in which the bodies lie above and behind the upper pole of the thyroid gland. This arrangement, however, is not constant, and occurs in a very small proportion of cases. In one instance, in which the body was found behind the upper pole of the left lobe of the thyroid gland, the blood supply came from the inferior thyroid artery. Other observers, notably Poole, of New York, have found that the parathyroid artery springs from the superior thyroid artery.

In every instance each parathyroid body is supplied by a distinct artery, which admits of definite isolation, and facili-

Fig. 1

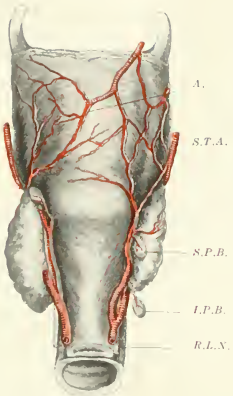


Fig. 2

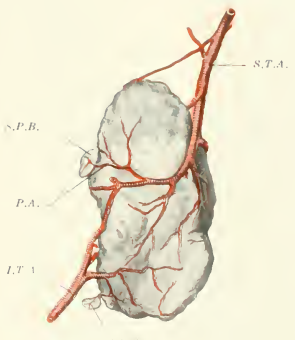


Fig. 1.—Posterior view of thyroid gland. Anastomosis between parathyroid bodies on both sides. *A.*, anastomosis in posterior surface of pharynx; *S. T. A.*, superior thyroid artery; *S. P. B.*, superior parathyroid body; *I. P. B.*, inferior parathyroid body; *R. L. N.*, recurrent laryngeal nerve. Reduced one-sixth natural size.

Fig. 2.—Left thyroid lobe viewed from behind. Shows unusual position and blood supply of superior parathyroid body, rendering body likely of removal in lobectomy. *S. T. A.*, superior thyroid artery *S. P. B.*, superior parathyroid body; *P. A.*, parathyroid artery; *I. P. B.*, inferior parathyroid body. Reduced one-sixth natural size.

tates the localization of the little body. It is often difficult, however, to observe this vessel because of its small size. The length of the parathyroid artery is too variable to justify any definite statement, but in cases in which the parathyroids are situated apart from the upper or lower poles of the thyroid gland the length of the artery may be almost a centimeter or more, and the slender twig may be more easily isolated, since the vessel invariably springs from the inferior thyroid artery before this artery enters the substance of the thyroid gland. In cases in which the parathyroids are found lying snugly against the gland substance on its posterior aspect the artery is shorter and, consequently, more difficult to isolate.

Practical Importance. The practical bearing of the anatomical relationship of these structures upon operations for removal of the thyroid gland is one of moment. The vascular supply of these little bodies is probably of most importance, since the integrity of the parathyroid artery must be preserved to ensure the vitality of the glandule in procedures dealing with ligation of the superior and inferior thyroid arteries.

Since it is often a matter of difficulty to isolate these bodies, even in careful dissections with complete exposure of the structures surrounding the thyroid lobes, with a field limited in size and partially obscured by slight hemorrhage and staining of the tissues in the operative field, it is obvious that failure will often attend the search for the parathyroids on the operating table.

Under such conditions, it is reasonable to assume that they will occasionally be sacrificed in spite of the most careful precautions taken to ensure their safety. The recognition of them during operation is obviously the surest means of avoiding their extirpation. In the event of failure to find them, due to the limitations of the field of operation, since these operations should be performed expeditiously; the most feasible method of ensuring their safety must be based upon our knowledge of their most constant location.

In the case of the superior pair of the glandulæ parathyroidæ, which often lie in such close proximity to the capsule of the thyroid and have a small and hardly perceptible artery supplying each glandule, it is difficult to understand how these little bodies can be preserved in lobectomy of the thyroid gland, or in ligation of the arterial trunk giving off the parathyroid branch.

The point to which in this communication I wish especially to draw attention, is the existence of a secondary or accessory blood supply to these small bodies. This seems to have escaped the notice of previous observers, as I have failed to find mention of it in the literature, with the exception of a suggestion that such anastomosis probably exists, thus explaining the failure of tetany to develop in certain cases of bilateral thyroidectomy. By turning to the illustrations it can readily be seen that even though a ligature be applied to the superior and inferior thyroid arteries *outside* the capsule, the parathyroid glandules may receive a very liberal blood supply through the anastomotic channels from the opposite side.

The histological characteristics of the parathyroid bodies undoubtedly afford a positive means of identification, but such proof is available only in the laboratory. It is doubtful whether recognition and isolation of the parathyroids can be made in any large proportion of cases at operation. Under such conditions the most trustworthy guide to their position is the recognition of the little parathyroid arteries running to these bodies, which vessels serve not only to locate them, but also to differentiate them from lymph nodes and remnants of thyroid and thymus glands.

In conclusion, it may be emphasized that of the relative importance of the arterial trunks to the thyroid gland, the inferior thyroid is probably of greater practical concern, since in a very large proportion of cases the parathyroid artery takes its origin from the inferior thyroid; consequently, it is the region of the entrance and distribution of this vessel to the gland substance that we must observe the greatest caution, in order to ensure the integrity of the vascular supply to the parathyroid bodies.

I desire to express my thanks to Professors Piersol and Frazier for their kind suggestions and advice, which so materially assisted me; to Drs. G. G. Davis and George Fetterolf for valuable advice; and to Mr. Erwin Faber for his excellent execution of the drawings.

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BOOK REVIEWS.

Röntgen Rays and Electro-therapeutics, with Chapters on Radium and Phototherapy. By Mihran Krikor Kassabian, M.D., Director of the Röntgen Ray Laboratory of the Philadelphia Hospital. Pp. 545. Philadelphia and London: J. B. Lippincott Company, 1907.

Dr. Kassabian deserves great credit for the completion and the presentation of this volume and for the labor involved in its compilation. It has been a task of no small magnitude, first of all, because of the wide scope of the subjects with which it deals. Secondly, the scarcity of collective literature, owing to the comparatively recent discovery of *x*-rays and the other agents under discussion, and the short time during which they have been employed for diagnostic and therapeutic purposes, have necessitated the collection of references from widespread sources, for the most part original articles in innumerable journals and society reports. Thirdly, the subject matter of a work of this kind must be confined largely to the particular interests of a comparatively small body of the medical profession.

The want of books of real intrinsic value dealing with the medical and surgical aspects of *x*-rays and allied subjects has been all too well recognized by radiographers and electrotherapeutists. Several books of this kind have been published already, but they have dealt almost exclusively with the Röntgen ray, giving but little space to other subjects such as electrotherapy, radiotherapy, and phototherapy. Dr. Kassabian's work, however, contains, primarily, a considerable amount of information that is of real practical value to the *x*-ray specialist, which is more than can be said concerning most books dealing with these subjects. It follows, therefore, that this work is one to be recommended as a good, reliable text book for beginners. The portion dealing with electrotherapeutics is especially valuable because it assists greatly in supplying the want of satisfactory and up-to-date literature upon this subject in a collective and concise form.

This volume is still more commendable because it is of value not to specialists alone, but to the entire medical profession, for it contains considerable data with which all practitioners should be familiar, but of which they seem to possess a woful lack of knowledge. In his introductory remarks the author mentions as one of his main objects the attempt to present the subjects in such form as to appeal to every practical physician.

The first part of the volume is devoted to electrotherapeutics, and begins with an introductory chapter on the elementary principles of electricity and magnetism in so far as they apply to medicine. These pages will be of particular value to the beginner, and, in addition, he will find useful suggestions that will assist him in search for such knowledge as he must acquire elsewhere. Subsequent chapters deal with static electricity, and the galvanic and the faradic or induced currents; the apparatus concerned in their production, and the methods of applying them. Additional chapters are devoted to the methods and principles concerned in cataphoresis, electrodiagnosis as applied to motor nerve and muscle degenerations, electrophysiology, and the practical application of electrical currents as therapeutic agents. Finally, it contains a valuable and concise chapter on high frequency currents.

The second part deals with the physics of Röntgen rays, the apparatus required for their production and its manipulation, the technique of fluoroscopy, radiography, and stereoradiography in connection with their use for diagnostic purposes. The subjects worthy of special mention are photography, *x*-ray apparatus, stereoradiography, and the medicolegal aspect of the Röntgen ray.

The third part deals with the practical application of the *x*-rays in the treatment of disease, and in addition there are several chapters devoted to phototherapy and radiotherapy.

This book deserves recognition as a standard work on the subjects with which it deals, and is to be recommended to the medical profession at large as well as to the specialist.

H. K. P.

A Practical Treatise on Fractures and Dislocations. By Lewis A. Stimson, B.A., M.D., LL.D. Fifth edition, revised and enlarged. New York and Philadelphia: Lea Brothers & Co., 1907.

The first edition of this work appeared in two volumes, one of which, published in 1883, was devoted to fractures, and the other, published in 1888, to dislocations. In 1899 the work was largely rewritten, and both subjects appeared together in one volume, in which form it has been continued.

The author has combined with a large experience a full and discriminating consideration of the literature of these subjects. He shows a rational tendency to adhere to the views and methods that have the sanction of the best authorities, and that have stood the test of long experience; hence, the work will be found a safe guide.

The size of the present edition has been increased by 32 pages and 58 new illustriations. The additional matter, and many of the illustrations relate to new evidence furnished by the *x*-rays. In fact, most of the additions and new matter have been made possible by advances directly dependent upon added information furnished by the *x*-rays. This is especially true of fractures of the small bones, like those of the carpus and tarsus, fractures near joints, incomplete and subperiosteal fractures. Much definite and valuable knowledge has thus been added.

The work has always been conservative, and the new edition maintains the same tone. For example, the fixation of fragments by open incision in cases of fracture is restricted to very few cases. On this point, the author says, "Direct fixation is very rarely necessary." And again, "Pins reaching to the exterior are also objectionable because of the difficulty of keeping their track aseptic; the infection may spread to the fracture." This stand is doubtless very well taken because a book of this kind reaches all classes of the profession, and if operations were freely advised the result would probably be to induce the inexperienced to resort too frequently to this method of treatment. While the tendency to direct fixation of fractures by operation is increasing, the most

radical surgeons agree that the conservative treatment must be employed if the most rigid asepsis cannot be secured.

An author is always confronted with the task of selecting from among the vast literature such views as his experience has shown to be sound, or as have the endorsement of the representative authorities on the subject. Naturally, this choice cannot satisfy all readers. In the case of the present work the selection seems sound and fair, as a rule; however, the reviewer regrets the absence of any reference to the splendid work of Allis on dislocations of the hip except two lines containing the mere statement that "attempts to reduce (a dislocated hip) were thought to have wound the (sciatic) nerve about the neck of the femur." The methods of Bigelow are quoted freely. In the reviewer's opinion Allis' work is as much superior to Bigelow's as the latter's work was to that of his predecessors, and, in fact, represents the only epoch-making demonstrations on dislocations since Bigelow's time.

The present volume has been brought up-to-date, and fully maintains the high standing of those that preceded.

A. C. W.

The Commoner Diseases of the Eye: How to Detect and How to Treat Them. By Casey A. Wood and Thomas A. Woodruff. Chicago: W. T. Keener & Co.

This is the third edition of this book, published first in 1904, and, judging by the present one, there will be, in all probability, a demand for others in the future.

It is of 600 pages, is well bound and fairly well illustrated, for though many of the drawings are rather crude and archaic, all are truthful and serve their purpose.

The book is issued as a manual for medical students and general practitioners, and as such is a very useful publication; it might be wise, if the authors wish to retain its elementary character, for them, in future editions, to use the blue pencil as well as to add new material, for if each edition has several new chapters it will soon cease to be a manual and become a text-book.

Indeed, there is now included much which it seems should be reserved for more advanced works on ophthalmology and for reading of those more interested in the special features of this branch of medicine than is the average student or general practitioner. For instance, there is too much operative technique considered, especially in regard to the removal of cataractous lenses, an operation which of all others, since it is a deliberate attempt to improve diminished vision, and for a condition which cannot be considered as needing immediate operative procedures, should be undertaken only by those making ophthalmology or at least surgery a special pursuit; if any operative details should be dwelt upon it seems that those for the relief of acute increase in the intra-ocular tension should be given the preference, for they, in many instances, admit of no choice of time or place, but must be attempted at once if vision is to be regained; yet these are described with no special stress on the essential features and with but one illustration, and that showing anterior sclerotomy.

The chapter on the more common injuries to the eye deals with them in a most satisfactor, manner, excepting the very important subject of Sympathetic Ophthalmia, which, while it is covered with thoroughness, has not the salient points emphasized to that degree which would catch and hold the attention of one not previously acquainted with them; for example, it seems that much more attention should be paid to the enucleation of the exciting eye, which at times is imperative and at others is useless and is even contra-indicated. The distinction is not sufficiently dwelt upon.

The chapter dealing with ocular hygiene is one which is very valuable and which is not frequently enough included in more pretentious works on ophthalmology; this, with those divisions considering the ocular complications and the ocular signs of certain general diseased conditions, would seem to be not only desirable but necessary for the general practitioner, who wishes the best results for his patients and himself, to know.

The addition which is by far the most important in this edition is the chapter by Dr. Frank Brawley, in which he considers the relation of ocular conditions to the surrounding nasal cavities. This discussion is most timely when so much is being written concerning the very close connection between these parts, and should be very helpful, since it is so easy to confuse their signs and symptoms.

Coming to the more distinctly local affairs of refraction and muscular anomalies, certainly enough is said, and it is extremely doubtful if even as much as is included is desirable unless a warning be appended that these are not the simple conditions the written words apparently indicate, and that every effort should be made to have them looked after by some physician at least fairly skilled in this line of practice.

H. M. L.

Elements of Human Physiology. By Ernest H. Starling, M.D.(Lond.), F.R.C.P., F.R.S., Jodrell Professor of Physiology, University College, London. Eighth edition. Chicago: W. T. Keener & Co.

It is pleasing to see the eighth edition of the work on physiology by Starling. The book, on the whole, is probably one of the most satisfactory that has ever been presented to the student of physiology. In these times, when text-books record the individuality of the author rather than the most important facts of physiology, this book deserves notice. The author's own work, which is extremely valuable, is given no more consideration than the work of others. Throughout he has buried his peculiarities in a desire to present that which is most valuable, and does this in a most satisfactory yet modest manner. The subject has never been presented in a clearer and more concise manner. The book gives sufficient material as a working basis for the medical student, and at the same time does not overwhelm him with theories, hypotheses, and the newer undigested material. The book will also be found equally valuable to the practitioner, who is compelled frequently to return to his physiological fundamentals for the interpretation of clinical phenomena. The illustrations are good and not overdone.

E. L.

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Through Dr. Morgan, the pupil of Hunter in London and of Cullen in Edinburgh, the graduates of this school take a just pride in regarding it as the lineal descendant of the best medical schools of Great Britain in the last century. To Dr. Morgan was soon joined another pupil of Cullen, Dr. William Shippen, as Professor of Anatomy and Surgery, thus forming another tie of relationship to the celebrated University of Edinburgh, whose methods of instruction were substantially adopted here. In the next year Dr. Adam Kuhn was added as Professor of Botany and Materia Medica; and in June, 1768, a "Commencement was held," at which medical honors were bestowed, the first in point of time in America. In 1769, Dr. Benjamin Rush was elected Professor of Chemistry, while Dr. Thomas Bond, one of the trustees of the College of Philadelphia, delivered lectures on Clinical Medicine in the Pennsylvania Hospital.

To the faculty thus composed of Morgan, Shippen, Bond, Kuhn, and Rush have succeeded, at various times, professors whose reputation has been national, such as Wistar, Barton, Physick, Chapman, Hare, Gibson Horner, Dewees, Jackson, George B. Wood, Hodge, James B. Rogers, Carson, R. E. Rogers, Leidy, Henry H. Smith, Pepper, Francis Gurney Smith, Stillé, D. Hayes Agnew, Goodell, W. Pepper, Jr., and Ashhurst.

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UNIVERSITY OF PENNSYLVANIA MEDICAL BULLETIN.

SYNOPSIS OF STUDIES IN METAZOAN PARASITOLOGY IN McMANES LABORATORY OF PATHOLOGY, UNIVERSITY OF PENNSYLVANIA.

By Allen J. Smith, M.D.,
Professor of Pathology, University of Pennsylvania.

The publication of statistical lists such as follows is more common in the journals of special scientific societies than in the usual medical journals; but in the present instance the writer hopes to justify himself by the fact that the Univ. of Penna. Med. Bulletin is the official organ of the institution in which these studies were made, and, too, by his desire to keep in proximity this list of records with the special descriptions of new parasites included and published in this same journal. For the most part, the parasites submitted for examination have, because of the correspondence of findings with already published descriptions, been merely named without other comment than the numbers of record and a statement of their habitat and host, and an acknowledgment of the person who collected the specimens. For further reference, should this in any case be desired, the reader may consult the books of the laboratory, in which the details of the various examinations are preserved. The value of such synoptical lists lies mainly in the aid they give parasitologists in determining the range of occurrence of parasites, the variety of hosts in which they have been met, and their habitat in the host; and it is for this reason that they should be of public record.

Much of the material has been placed at the disposal of the writer by the Laboratory of Comparative Pathology of the Philadelphia Zoölogical Gardens, the specimens having for the most part been obtained at autopsy of animals which have died in the Gardens during the service of Dr. C. Y. White as pathologist, or of Dr. Herbert Fox, his successor. A number were collected by Dr. J. J. Repp, in Iowa; others were obtained from the hospital of the Veterinary Department of this university; and the remainder, mainly parasites from the human body or from laboratory experiment animals, have been referred by various physicians or were collected by the writer. The list includes studies made since 1903, but is by no means a complete one, as in the early part of the intervening period such parasitological studies were not recorded save occasionally, and since then often no record has been made of common and well-known specimens. The numbers in brackets refer to the accession books of the laboratory ("Path. Hist., —") or museum ("Path. Mus., —"); and, when known, the number of the host in the records of the laboratory of the Zoölogical Gardens ("P. Z. G. Lab., —") is also indicated to facilitate reference.

A. VERMES.

I. *Trematodes.*

1. *Echinostoma ferox*, Rudolphi (Path. Hist., 1110), from the small intestine of a stork, *Ciconia ciconia* (P. Z. G. Lab., 805). The entire small intestine was invaded, the parasites being quite numerous. The heads of the flukes were embedded in the wall of the gut in small cavities, the tissue about which was swollen and the seat of marked inflammatory reaction, the lesions protruding on the serous side of the wall like miliary tubercles. This mode of attachment varies from that usually stated, which would have the worm attached by its ventral sucker to the interior of the small cavity in the intestinal mucous membrane and both cephalic and caudal ends protruding above the surface of the lining of the gut. The only other point of difference from the current descriptions of the parasite which was noted was the absence of the cuticular spines from the anterior portion of the worm (not about the mouth, however); but these, according to Dujardin, are very caducous.

This was the second stork of the same species to die in the Gardens since the establishment of the Laboratory of Comparative Pathology with these parasites in the intestine. Both birds were newly arrived in the Gardens, one dying within twenty-four hours after its reception, and the other, the host of the specimens examined, within seventy-two hours.

2. *Paragonimus westermanni*, (Kerbert) (Path. Mus., 39), from the lung of a mouse, presented by Professor Katsurada, of Okayama, Japan, is identical with the lung fluke of man of the same part of the world.

3. *Opisthorchis sinensis*, (Cobbold); three specimens, one from the gall ducts of a human being and the others from the gall ducts of dog and cat; presented by Professor Katsurada, Okayama, Japan.

4. *Monostoma mutabile*, Zeder (Path. Hist., 1132, 1654), has been obtained in one instance from the subpleural air spaces of a coot, *Fulica americana* (P. Z. G. Lab., 885), and in a second case from the liver (this statement is made with uncertainty in the records of the laboratory of the Gardens; it is probably incorrect, and it is more likely that the worms were in the subperitoneal airspaces) of a Carolina rail, *Porzana carolina* (P. Z. G. Lab., 917). The data of identification of both groups of the parasite conform with published descriptions; but the ova were considerably smaller than the measurements given by Dujardin and repeatedly followed in later works upon parasitology. Dujardin (*Hist. Nat. des Helminthes*, p. 351; Paris, 1845) states that the ova are 0.173 mm. in length and 0.084 mm. in breadth; those obtained from the parasites of the first of the above birds measured 0.110 to 0.120 mm. in length and 0.075 to 0.080 mm. transversely, and those from the parasites of the second bird 0.105 to 0.120 mm. in length and 0.060 to 0.080 mm. transversely.

II. *Cestodes.*

(*a*) *Larval or Bladderworm Stage.*

5. *Cysticercus fasciolaris* (bladderworm of *Tænia crassicolis*, Rudolphi, of cat) is recorded four times: once in the liver of a muskrat, *Fiber zibethicus* (L.), killed at Kennett Square, Pennsylvania, and presented by Dr. I. H. Alexander (Path. Mus., 169); twice (Path. Hist., 1652) in the livers of white experiment rats in the laboratory and in Wistar Institute; and once in the liver of a white mouse, presented by Mr. Howard Crawley. In all cases these bladderworms were present in numbers, the liver of the muskrat containing several hundreds and being enormously enlarged in consequence.

6. *Cysticercus tenuicollis* (bladderworm of *Tænia marginata*, Batsch, of dog) was encountered twice (Path. Mus., 44, 45) in the subperitoneal tissue of the domestic sheep, *Ovis aries;* two examples from the same host having been obtained in Iowa by Dr. Repp; and a third, a single occurrence, from the dressed carcass of a sheep in one of the Philadelphia markets, by one of the veterinary medical students. Recently Professor Joseph McFarland, of the Medico-Chirurgical College of this city, submitted to the writer a fourth example which he had obtained from the subperitoneal tissue of a goat, *Capra hircus*.

7. *Cysticercus cellulosæ* (bladderworm of *Tænia solium*, Rudolphi, of man) was submitted for identification (Path. Mus., 29) in the flesh of a domestic hog, *Sus scrofa*, by Dr. J. W. Nixon, of Gonzales, Texas. Once before, in Texas, pork has been found infested by this larva by the writer. It may be added, however, that, out of some dozens of tapeworms from the human intestine which the writer has examined in this part of the country and in Texas, none have ever proved to be *Tænia solium*, although the belief is common that this species is of frequent occurrence in man in America. Doubtless the parasite occurs in this country, as is indicated by the above experience with the bladderworm stage; but it is much less frequent than is usually believed, specimens of the beef tapeworm, *Tænia saginata*, being confused with it by mistake.

8. *Cysticercus pisiformis* (bladderworm of *Tænia serrata*, Goeze, of dog), obtained at Galveston, Texas, by Dr. J. J. Terrill from the liver of a common laboratory rabbit, *Lepus domesticus* (Path. Mus., 20).

9. *Hydatid cysts* (bladderworm stage of *Tænia echinococcus*, v. Siebold, of dog) have twice been received for study. In one instance several daughter cysts and a portion of the mother cyst wall of a large subperitoneal hydatid (Path. Hist., 1900) from a man, a native Pennsylvanian, a patient in the Scranton State Hospital, at Scranton, Penna., by Drs. J. Cohen and T. O. Williams. The daughter cysts submitted were barren, but showed the remnants of the cestode heads; they were unusually large, being between three and four centimeters in diameter. The second example (Path. Hist., 1717) was met in the lung of a gazelle, *Gazella dorcas* (P. Z. G. Lab., 1145). The cyst and contained daughter cysts in this instance were of the usual type, and numerous examples of echinococci and their hooklets were met in the examination.

10. *Pterocercoids* of an unknown bothriocephalus (Path. Hist., 1691) were obtained from the liver of a wood ibis, *Tantalus loculator* (P. Z. G. Lab., 960). There were five of these larvæ in the host. The usual rule for such larval bothriocephalus worms is that they occur in fish or other habitants of water and later develop to adult stage in another host devouring the fish; but while it is unusual to meet with them in the present type of host, it is neither impossible nor unknown, and it is to be presumed that the free-swimming embryo was obtained by the bird with water swallowed.

(*b*) *Adult Cestodes.*

11. *Tænia serrata*, Goeze (Path. Mus., 31), obtained several times from the small intestine of dogs used in the experimental work of the laboratory, several examples, as a rule, from each host.

12. *Tænia saginata*, Goeze (commonly known as *Tænia mediocanellata*, Küchenmeister): this, the ordinary "beef tapeworm," from the human intestine, has been brought

into the laboratory at least seven or more times within the past few years from this State or from New Jersey (Path. Mus., 27; Path. Hist., 151, 978, 1651), although not all of these are recorded. One example, presented by Dr. David Edsall, was one of six strobiles met at autopsy in the intestine of a Syrian woman who died from tuberculosis in the Phipps Institute of this city. Two entire strobiles were submitted by Dr. P. S. Stout, who obtained them from living patients after the use of a taeniafuge. The other instances were fragments found in the dejecta and sent to the laboratory for indentification before treatment.

13. *Tænia crassicolis*, Rudolphi (Path. Hist., 1106), has been identified from the ileum of an eyra, *Felis eyra*, which died in the Zoölogical Gardens from an intense acute enteritis. Along with it there were also met in the upper part of the intestine a number of examples of *Uncinaria canina*. The single specimen of tapeworm was immature, the strobile measuring 16.5 cm. in length and including no ripe links. The general features of the worm, save in the fact that the measurements of the head and of its hooklets and of the individual proglottides were lower than those usual to this worm, were quite in conformity with the known characteristics of *Tænia crassicolis*; but it is possible that in this type of cat a special variety of the parasite in question may develop and may be represented by the present example.

14. *Tænia paradoxuri*, n. s. (Path. Hist., 1714), passed in the dejecta from living paradoxure, *Paradoxurus grayi*, in the collection of the Zoölogical Gardens. For detailed description, see special article in this journal (p. 283).

15. *Tænia cuneetes*, n. s.; a number of examples (Path. Hist., 1694) were obtained from the small intestine of an anaconda, *Eunectes murinus* (P. Z. G. Lab. 939). For description, see special article in this journal (p. 283).

16. *Tænia unilateralis*, Rudolphi (Path. Hist., 1681). Along with two species of nematodes there were found in the intestine of a blue heron, *Ardea herodias* (P. Z. G. Lab., 1158), a number of fragments of the strobile of what the writer believes to be Rudolphi's incompletely described *Tænia unilateralis*. The heron, a North American species, died within a week after its reception in the Gardens. The head of the tapeworm was missing from the material obtained, and none of the links examined contained ova. The largest segments measured 2 mm. in width and 0.2 to 0.4 mm. long, were trapezoid in form, with the posterior margin thick, crenulate, and prominent. These proglottides have not as yet been sectioned for microscopic examination; but it may be stated that the genital pores are all on one side, that the cirrus is long and lies coiled in its sheath, extending from the pore (in the anterior part of the lateral border of the link) along the anterior portion of the segment nearly to the median line, and that the vagina opens posteriorly in the genital pore, and its tube is traceable toward the median part of the segment. The details of the rest of the genital apparatus are, however, uncertain without histological examination.

17. *Monieza expansa*, (Rudolphi), from the intestine of sheep, *Ovis aries*, collected in Iowa by Dr. J. J. Repp (Path. Mus., 25).

18. *Monieza planissima*, Stiles and Hassal (Path. Mus., 30), from the intestine of sheep, collected in Iowa by Dr. J. J. Repp.

19. *Thysanosoma actinioides*, Diesing (Path. Mus., 26), from the intestine of sheep, *Ovis aries*, in Iowa, by Dr. J. J. Repp.

20. *Ctenotænia leuckarti*, (Rheim) (Path. Hist., 1797), from the intestine of a cotton-tail rabbit, *Lepus sylvaticus*, killed near Philadelphia, collected by Dr. H. C. Masland.

21. *Dipylidium caninum*, (Linn.), has been met a number of times in the small intestine of dogs in the laboratory, usually two, three or more in a single host (Path. Mus., 32); and once (Path. Hist., 1065) in the intestine of a domestic cat in the hospital of the Veterinary Department of this university (Vet. Hosp., 1330). This last example is by some regarded as a separate species, and described under the name *Tænia elliptica;* but aside from the usually smaller size of the strobile and proglottides and the slightly larger size of the ova, does not materially differ from canine examples and is at most a mere variety (*D. caninum*, var. *cati*).

22. *Cotugnia browni*, n. s. (Path. Hist., 1672), from the intestine of a banded parrakeet, *Palæornis fasciatus* (P. Z. G. Lab., 1052). For description see special article in this journal (p. 284).

23. *Hymenolepis nana*, (v. Siebold). These specimens (Path. Mus., 5), including in all over a thousand strobiles, were obtained by Dr. L. E. Magnenat from the stools of three children in Amarillo, Texas, after administration of male fern. The hosts were all from the same family, and later Dr. Magnenat found a fourth child in the same family also infested. The ova had been detected in the feces by the physician. Probably many strobiles escaped notice in collection of the material, and the total number in the intestines was surely greater than represented by the material in hand, as Dr. Magnenat subsequent to the medication found numerous ova persisting in the stools of his patients.

24. *Hymenolepis diminuta*, (Rudolphi) (Path. Hist., 1646), from the intestine of a Texas cotton rat, *Sigmodon hispidus texianus* (P. Z. G. Lab., 1096). The material submitted in this instance was fragmentary, and no heads were included; and the identification, therefore, is not absolute. The general features agree closely with those accepted for *H. diminuta* save in the one fact that filaments are to be recognized in the middle layer of the covering of the ova, arising, as in *H. nana*, from polar tubercles on the inner wall. There is, however, too much divergence in the segments to permit the identification with *H. nana*, and the

writer is disinclined to regard the peculiarity of the ova noted as sufficient basis for separating these specimens as a novel species.

25. *Davainea cesticillus*, (Molin); numerous examples in the intestine of domestic fowl, *Gallus gallinaceus*, collected by Dr. S. H. Grant, Rugby, Texas (Path. Mus., 22).

26. *Dibothriocephalus latus*, (Linn). The fish tapeworm of man has been met in the work of the laboratory three times within the past few years. Dr. William Pepper (Path. Mus., 170) obtained, after recognition of the ova in the stool and the administration of an anthelmintic, an entire strobile in the dejecta of a Norwegian sailor in the University Hospital in 1905. Dr. R. N. Willson, in 1906, referred to the laboratory a portion of a strobile of the parasite (Path. Hist., 852) which he had obtained after administration of an anthelmintic from the feces of a young male Polish student in the University of Pennsylvania; and in the spring of 1907, Dr. C. LeR. Griswold, then a fourth-year medical student, obtained a meter or more of the strobile of the same species of tapeworm (Path. Hist., 1822) from another student. The host in this last instance was an American, but had spent his previous summer vacation in European travel; and as all the symptoms suggestive of parasitism had followed this European sojourn, it is possible that this, too, was an instance of the importation of the worm.

A number of fragments of what the writer believes to be the same parasite (Path. Hist., 1454) were found in the large intestine of a gray fox, *Canis cinereo argentatus* (P. Z. G. Lab., 1001). The head was not found in this case. The anatomy of the links corresponds closely with the recognized structure of proglottides from man, but the ova are distinctly smaller than those from the worm from human subjects (averaging 0.054 mm. long and 0.030 mm. transversely) and are slightly more pointed toward the operculated end. An interesting reaction was noted when sulphuric acid was run under the coverglass of a water preparation containing these ova for the purpose of separating the lid, the interior of the eggs invariably assuming a pink to red color, very like the well-known "cholera red reaction" with stools of Asiatic cholera and doubtless due to the same cause, the presence of indol. The absolute identification of the material is, of course, not to be insisted upon, but the writer believes the specimens to be a variety or in very close relation to *Dibothriocephalus latus*. The host was an American fox, but it is not known from what part of the country it originally came.

27. *Bothridium pythonis*, Blainville (= *Solenophorus megalocephalus*, Creplin), has been obtained several times (Path. Mus., 40; Path. Hist., 774) from pythons; once from the intestine of a *Python molurus*, at autopsy, in the Zoölogical Gardens, and again in the dejecta of a living *Python reticulatus* in the collection of the Gardens. Numerous examples were found in the material from each snake (*cf.* article on Solenophorus megalocephalus by Smith and Veeder, *Trans. Phila. Path. Soc.*, 1905). Recently another lot of these same worms have been sent to the laboratory from the Gardens, having been discharged together with a large number of ascarides from a *Python reticulatus*, but as yet these have not been fully studied and recorded, and are not included in the present series.

III. *Nematodes.*

28. *Ascaris lumbricoides*, Linn., from the human intestine, has been submitted to the laboratory a number of times (among others, Path. Mus., 38; Path. Hist., 1179), most of which have unfortunately not been recorded. Among those not placed of record was one vomited by a child in the early part of an attack of measles, and in the same family several days earlier another child with the same infectious disease passed several of the worms *via recti*. The voidance of intestinal parasites in the course of acute infectious fevers is by no means an uncommon occurrence; it is thought to be possibly due to a deleterious action of the toxins of the disease upon the parasites, causing them to lose whatever attachment they may have had to the intestinal wall, or weakening or killing them and thus permitting them to be swept with the discharges from the canal. Some years ago a similar experience was met by the writer in the case of a young man who was known, from the discovery of the ova in his stools, to be the host of *Uncinaria americana*, Stiles. The ova had been repeatedly observed in the feces until an attack of smallpox intervened. Shortly thereafter, and continuously from the time of the variola, no more ova could be detected in the excrement, the presumption being that the parasites had been lost during the febrile period.

29. *Ascaris equorum*, Goeze (= *A. megalocephala*, Cloquet), was met twice in the present series, once (Path. Hist., 775) passed in the dejecta of a Burchell zebra, *Equus burchelli*, in the collection of the Zoölogical Gardens, and the second specimen picked up in the street by one of the medical students, Mr. O. H. P. Pepper, where, doubtless, it had been deposited by some passing horse.

30. *Ascaris canis*, (Werner) (= *A. mystax*, Zeder), has been repeatedly met in the intestines of dogs used in experimental work in the laboratory (Path. Mus., 33); was referred in one instance (Path. Mus., 14) by Dr. J. J. Repp from a dog in Iowa; was found (Path. Hist., 1447) in the intestine of a chow-dog, the hairless Chinese dog, *Canis domesticus sinensis* (P. Z. G., 1015); and in large numbers from the intestine of a puppy which died in the veterinary hospital of Dr. Horace Hoskins, in this city.

It is generally accepted that the examples of this type of worm met in cats are identical; although it is true that minor

differences have been noted and that the feline specimens are often spoken of as constituting a separate variety, *A. canis*, var. *cati*. In the list of laboratory studies specimens are recorded from the domestic cat, *Felis catus*, from Texas (Path. Mus., 18) and from Philadelphia from the veterinary hospital of this university, and also from a jaguarundi (Path. Hist., 1662), *Felis jaguarundi* (P. Z. G. Lab., 1157), received from a dealer, shortly before its death, into the collection of the Zoölogical Gardens.

31. *Ascaris leptoptera*, Rudolphi. Under the name *Ascaris leptoptera* round worms closely related to *Ascaris canis* have been described from a number of the larger cats, but there has always existed a lack of uniformity of description, which has long given the idea that several varieties and possibly several species have been confused under the name. Two instances of these parasites are included in the present list, both from lions (Path. Hist., 1102, 1148), in one case obtained at autopsy from the stomach and intestines of a lioness (P. Z. G. Lab., 794), and in the other found in the feces of a living lion in the collection of the Zoölogical Gardens. The worms from the two animals are identical, and to the writer's mind present sufficient peculiarity to permit them to be regarded as constituting a new variety. For full description, see special article in this journal (p. 285).

32. *Ascaris aquillæ*, n. s. (Path. Hist., 1637), from the proventricle of a bald eagle, *Haliætus leucocephalus* (P. Z. G. Lab., 959). For description of these specimens, see special article in this journal (p. 287).

33. *Ascaris serpentulus*, Rudolphi (Path. Hist., 1683), from the intestine of a demoiselle crane, *Anthropoides virgo* (P. Z. G. Lab., 1165), a European crane which had been in the Gardens for about three months.

34. *Ascaris ardeæ*, n. s. (Path. Hist., 1681), from the intestine of a blue heron, *Ardea herodias* (P. Z. G. Lab., 1158). This bird was also the host of the *T. unilateralis*, Dujardin, above mentioned (16) and an undescribed species of dispharagus. For detailed description, see special article in this journal (p. 287).

35. *Ascaris rubicunda*, A. Schneider (Path. Hist., 1677), in large numbers from the intestine of an Indian python, *Python molurus* (P. Z. G. Lab., 1122).

36. *Ascaris anoura*, Dujardin (Path. Hist., 773), passed in large numbers with the feces of a living python, *Python reticulatus*, in the collection of the Zoölogical Gardens.

37. *Heterakis papillosa*, (Bloch) (Path. Hist., 1645), from the cæca of a golden pheasant, *Chrysolophus pictus* (P. Z. G. Lab., 1055).

38. *Heterakis perspicillum*, (Rudolphi) (Path. Mus., 21), from the intestine of domestic fowl, *Gallus gallinaceus*, collected by Dr. S. H. Grant, in Texas. Another, but unrecorded, instance of this parasite was submitted for identification by Dr. L. L. Powell in the summer of 1905, the worm having been found in an egg of a domestic fowl in this city. Such inclusions of intestinal worms in eggs usually creates considerable wonderment, but is no very rare occurrence. The worm, passing by way of the cloaca of the fowl into the oviduct, comes to be mingled with the albumen and encased by the shell of the egg.

39. *Oxyuris vermicularis*, (Linn.) (Path. Mus., 4), is recorded as met in numbers in an appendix vermiformis removed by Dr. J. G. Clark from a woman in the University Hospital, the parasites having very possibly been an important factor in exciting the symptoms of appendicitis leading to operation. In addition to this instance a number of other groups of the same worm have been submitted for identification from time to time, but for some reason, presumably because of their frequence and ease of recognition, were not recorded.

40. *Oxyuris equi*, Schrank (Path. Mus., 8), collected by Dr. J. J. Repp, in Iowa, from the colon of a horse, *Equus caballus*.

41. *Oxyuris megatyphlon*, (Rudolphi) (Path. Hist., 776), from the large intestine of an iguana, *Iguana tuberculata*, in the collection of the Zoölogical Gardens.

42. *Oxyuris microtyphlon*, n. s. (Path. Hist., 1121), from the large intestine of a Cuban iguana, *Cyclura nubila* (P. Z. G. Lab., 827). For detailed description, see special article in this journal (p. 288).

43. *Oxyuris curvata*, Linstow (Path. Hist., 1636), from the small intestine of a Canada porcupine, *Erethizon dorsatus* (P. Z. G. Lab., 991). Linstow (*Mitth. Mus. Berlin*, i, heft 2, p. 20) has described from *Hystrix brachyura* (?) an oxyuris apparently the same as the specimens here recorded; but so far as is known to the writer the present instance is the only one, aside from Linstow's original observation, in which these parasites have been recognized, and inasmuch as Linstow's record is extremely brief the description entered in the laboratory records from the material in hand seems worthy of full publication. Linstow found his material in the zoölogical collection of the Berlin Museum of Natural History labelled as obtained from *Hystrix brachyura*, but in a footnote to his communication manifests uncertainty as to the correctness of the specific name of the porcupine. He states in brief that only female examples were present, which measured 9.1 mm. in length and 0.47 mm. in thickness; that the esophagus, which ends in a bulb, measured 1 : 11.5, and the long pointed tail 1 : 7.7 of the body length of the worm; that the vagina of the specimens projected as a thick tube 0.22 mm. in length and 0.044 mm. thick; and that the cuticle at the head end was swollen out in a fusiform manner.

The notes of laboratory study (Plate I) of the writer's material, made July 22, 1907, are as follows: From the small intestine of this animal (Canada porcupine) were obtained fifteen small nematodes, all female and non-gravid, the

largest (Fig. 1) measuring 8 mm. in length and 0.5 mm. in thickness at thickest level (about 2 mm. from head end), the smallest about half this size. Specimens nearly round in section; tapering anteriorly to the head, which at base of lips measures from 0.07 to 0.09 mm. in diameter; tapering more gradually posteriorly to a long slender tail ending almost effilate, as in oxyuris. Cuticle thin and transparent, finely striated transversely (striæ 0.01 mm.); at head end two cuticular swellings (Figs. 2 and 3) of small size one on either side of base of dorsal lip; and back of lips cuticle of head end slightly swollen in fusiform manner. The body wall, from about the level of the esophageal bulb, shows two longitudinal ventrolateral granular bands (apparently not cuticular, but due to the granular muscles showing through the cuticle). Three nearly equal lips (Fig. 3), each with a ridge from base to tip, this ridge at base, near middle of lip, and at the margin, showing special thickenings. Opposite the intervals between these lips and reaching in each case to near the middle of the lips the cuticle extends forward like an outer set of lips, each with five marginal lobes. On either side of dorsal lip, outside the last-named structures, is seen a more or less lobulate but small cuticular swelling. When seen from the side these various lobate protrusions and the lips give a coarsely fringed appearance to the front of the head. The esophagus (Figs. 1 and 4), measuring a little more than 1 mm. in length (including the bulb), is at first nearly uniform in diameter and slender (0.08 mm. in diameter), but gradually thickens in flask-like manner until at a level of 0.8 mm. from the lips it has attained a diameter of 0.17 mm., just back of which it contracts, and from this constriction forms a spheroidal bulb (0.2 mm. long and 0.23 mm. in diameter). Transverse section (Fig. 5) shows a triradiate esophageal lumen; within the bulb a three-toothed (?) armature. For about 1 mm. beyond the bulb the intestine is thick (0.2 to 0.25 mm.), after which it narrows (0.15 to 0.1 mm. or less), running a straight course to the anus. In the rectum it again expands in a fusiform manner; and at the posterior portion of this part of the tube are attached several large monocellular anal glands. Anus situated 1.4 mm. from the tip of the tail. Vulva at one-third of body length from the head (2.5 mm. in an 8 mm. example). In all of the specimens the vagina (Figs. 1 and 6) projects as a thick finger-like tube beyond the body wall, covered on the outside with cuticle and with the central lumen surrounded by what seems to be a layer of circularly disposed muscle cells. In specimen of 8 mm. length, this vaginal extension measured 0.4 mm. in length; and in all the rest of the specimens in hand it bears similar proportions. At the distal end it is subdivided, the lumen opening between the two lateral lobes. Within the body the vagina extends posteriorly an equal distance (about 0.4 mm.) before opening into the uterus; uterus simple, extending posteriorly (2 mm. in length in the specimen measured), and showing one, two, or three cyst-like dilatations in its course. The dilatations mentioned are variable in size as well as in number, but may reach above 0.2 mm. in width and 0.5 mm. in length. While in the non-dilated parts of the uterine canal (diameter about 0.05 mm.) the wall is thick, rather opaque, granular, and yellowish, and closely crowded with cells, the walls of these cyst-like expansions are very thin, transparent, without appreciable color, and made up of large flat cells very like the endothelial cells of mammals. At its posterior extremity the uterine tube narrows to a blunt point, into which the two ovarian tubes enter. The latter are to be seen passing forward from this point, tortuously plicated along the posterior two-thirds or three-fourths of the uterus, then leaving the uterus to extend forward along the body wall ventrally and dorsally nearly to the level of the vaginal protrusion, and ending in a large geniculate ovarian tube apparently attached to the body wall. No trace of ova or of larval worms were met in any of the specimens (all examined closely for this feature).

At first the peculiar protrusion of the vaginal tube was supposed to be the result of artefact, but careful study soon satisfied the writer that it constituted a constant and specific feature; and no suggestion of similarity to allantonema could be entertained. Tentatively the name *Oxyuris evaginata* was applied in the records to the specimens, but subsequent examination of the literature has fixed the prior recognition of the worm to Linstow, and compelled the retraction of the writer's provisional name and the adoption of that employed by Linstow. The singularity that in both Linstow's material and that of the writer only female specimens were encountered is striking; and it is possible that the virgin state of the specimens may have some bearing, as yet unappreciated by the writer, upon the peculiar vaginal evolution.

44. *Strongylus filaria*, Rudolphi (Path. Hist., 1680), from the bronchial tubes of a bison, *Bison americanus* (P. Z. G. Lab., 289).

45. *Strongylus paradoxus*, Mehlis (Path. Mus., 15), from the bronchial tubes of a domestic hog, *Sus scrofa*, collected in Iowa by Dr. J. J. Repp.

46. *Œsophagostoma inflatum*, (A. Schneider), (Path. Hist., 1673), met along with several specimens of an unknown globocephalus in the lumen and in several tiny submucous cysts in the wall of the intestine of a pig-tailed macaque, *Macacus nemestrinus* (P. Z. G. Lab., 508).

The worms, one male and four females, are colorless, cylindrical on section, rigid, opaque; cuticle finely striated transversely. They are of nearly uniform thickness in the greater part of the body length, tapering slightly anteriorly to a head about a quarter as wide as the body of the worm, tapering posteriorly less rapidly to the tail. Mouth terminal, circular, surrounded by a chitinous ring with the cuticle over this elevated into a prominent cir-

cular lip. Upon the latter six rather long, pointed papillæ. Posterior to this lip the cuticle of the head is expanded into a collar extending for about one-third the length of the esophagus, sharply defined posteriorly by dorsal and ventral depressed transverse lines. From the level of these on each side a narrow alar cuticular expansion, in which there is situated a pointed papilla (opening of cervical glands). No buccal cavity or capsule, the esophagus beginning immediately back of the mouth opening. Esophagus flask-shaped, relatively short; intestine large, with thick cellular wall, the columnar cells of which show especially distinctly posteriorly. Anus subterminal in both sexes. The largest female measures 16 mm. in length and 0.45 mm. in thickness at middle. Tail obtusely conical, with mucronate tip. Anus 0.2 mm. from tip of tail. Vulva prominent, with thick circular lip, situated 0.35 mm. anterior to anus. Double ovarian tube. Ova yellowish, elliptical, with single, smooth, colorless shell, and with interior often segmented; measures 0.06 to 0.08 mm. in length and 0.044 to 0.048 mm. in transverse diameter. The measurements of the head structures follow: transverse diameter of circular lip, 0.1 mm.; of chitinous ring underlying this lip, 0.06 mm.; diameter of oral opening, 0.02 to 0.03 mm.; length of collar about neck of worm, 0.26 mm., transverse diameter of same, 0.28 mm.; length of esophagus, 0.7 mm., with a transverse diameter in its posterior portion, 0.2 mm.; lateral cervical papilla 0.17 mm. posterior to this collar.

The single male example included in the material measures 14.5 mm. long, and at middle of length 0.45 mm. in thickness. Tail obtusely conical, ending in a bilobed bursa (with indistinct ventral lobe), not much wider in lateral (0.6 mm.) than in dorsoventral measurement (0.4 mm.). Dorsal ray deeply bipartite, its divisions widely curving from one another, each with a single, simple, small branch near root; dorsomedian ray simple, arising at base of dorsal ray; lateral and ventrolateral rays from a common base, the former divided; ventral ray divided. Just above the level of the cloaca a small ray or papilla from the body wall. Cloaca 0.2 mm. from tip of tail. Two equal, long, pliant spicules, 1.3 mm. long and protruded in the specimen examined 0.9 mm. Anterior end of male as in female.

Comparison of these features with those of known œsophagostomes would indicate a close relation with *Œ. inflatum* (A. Schneider), if not entire identity. In many respects it agrees well with Linstow's *Strongylus aculeatus* (*Württemb. Jahresb.*, 1879, p. 333) from a macaque monkey, but the mouth parts are distinctly different (in the presence of the cervical collar and in the absence of the two lateral teeth in the mouth); and both anteriorly and in the details of the male tail it differs distinctly from Molin's *Œsophagostoma pachycephalum* (*II sottordine degli Acrofalli, p.* 450) of a cercopithecus. While the host in this case is far removed from the ordinary host of *Œ. inflatum* (large intestine of beef), the correspondence of structure is so great as to make the writer unwilling to regard it as constituting a separate species. This detail of description is here inserted for reference, inasmuch as the occurrence of the worm in such unusual situation may excite question as to the correctness of identification.

47. *Globocephalus macaci*, n. s. (Path. Hist., 1673), met along with the immediately preceding parasite in the intestine of a pig-tailed macaque, *Macacus nemestrinus*. For description, see special article in this journal (p. 290).

48. *Sclerostoma equinum*, (F. Muller) (Path. Mus., 9), from the subperitoneal tissues of a colt, *Equus caballus*, in Iowa, collected by Dr. J. J. Repp.

49. *Syngamus trachealis*, v. Siebold (Path. Hist., 1108), from the trachea and bronchial tubes of a young Reeves' pheasant, *Phasianus reevesi*, killed in the Zoölogical Gardens to prevent development of an epidemic of the "gapes."

50. *Uncinaria duodenalis*, (Dubini) (Path. Mus., 2; Path. Hist., 148), obtained at autopsy from the upper part of small intestine of human being; two cases, both white men and both Europeans, the first in Galveston, Texas, the second in the Philadelphia Hospital.

51. *Uncinaria americana*, Stiles (Path. Mus., 1), obtained after administration of thymol from the dejecta of human being in Galveston, Texas. Two instances of this parasite have been brought to the laboratory from the University Hospital and from the Philadelphia Hospital for identification of the ova, and subsequently for verification of the worms, but neither of these are included in the records of the laboratory.

52. *Uncinaria canina*, (Ercolani), is comparatively common in the intestines of dogs used in the laboratory for experimental purposes, some animals being heavily infested. It is recorded in the laboratory notes also from the dog, *Canis domesticus*, from Galveston, Texas (Path. Mus., 24); from the duodenum and jejunum (Path. Hist., 1106) of an eyra, *Felis eyra;* from the duodenum (Path. Hist., 1662) of a jaguarundi, *Felis jaguarundi* (P. Z. G. Lab., 1157); and (Path. Hist., 1643) from the small intestine of a gray wolf, *Canis mexicanus nubilus* (P. Z. G. Lab., 919).

53. *Physaloptera turgida*, Rudolphi (Path. Hist., 1656, 1660, 1685), from the stomach of the common opossum, *Didelphis virginiana*, from the Wistar Institute of Anatomy and from the Zoölogical Gardens (P. Z. G. Lab., 324, 1166).

54. *Trichuris trichiura*, (Linn.), is recorded from the colon of man (Path. Mus., 3; Path Hist., 148) in the records of the two autopsies above referred to (50) under *Uncinaria duodenalis*. Ova of this worm have also been identified several times in the stools of human beings (unrecorded).

55. *Trichuris suis*, (Schrank) (Path. Mus., 16), from the large intestine of the domestic hog, *Sus scrofa*, collected in Iowa by Dr. J. J. Repp.

56. *Trichuris vulpis,* (Frölich) (Path. Mus., 35), from the large intestine of dog, *Canis domesticus,* in the laboratory.

57. *Trichuris ovis,* (Abildgaard) (Path. Hist., 1901), from the large intestine of an antelope, *Antelope furcifer,* in the Zoölogical Gardens.

58. *Trichinella spiralis,* (Owen), has been met three times (as the encysted larval worms) in human muscle, having been once submitted (Path. Mus., 37) in a portion of the pectoral muscles of a badly infested human cadaver in the dissecting-room by Dr. J. K. Pollock, then a medical student of this school; and twice having been found (Path. Hist., 189, 358) in the muscle of the diaphragm in autopsy material from the Philadelphia Hospital.

59. *Filaria immitis,* Leidy (Path. Mus., 6), from the right heart and pulmonary artery of a dog used in experimentation in the laboratory.

60. *Filaria equina,* (Abildgaard) (Path. Mus., 19), from the peritoneum of a horse, *Equus caballus,* collected in Iowa by Dr. J. J. Repp. A second specimen was presented by Dr. Repp, a single male example, which was taken from the anterior chamber of the eye of a horse in Iowa (Path. Mus., 7). The name *Filaria oculi* has been attached to such examples; but the anatomy of the specimen leaves no doubt in the writer's opinion that this is merely an aberrant example of the species here named.

61. *Filaria labiato-papillosa,* Alessandrini (Path. Mus., 17), was collected by Dr. J. J. Repp, in Iowa, from the peritoneum of a cow, *Bos taurus.* A single example (Path. Hist., 1675) was sent into the laboratory from the Zoölogical Gardens labelled as having been found in the body of a bison, *Bison americanus* (P. Z. G. Lab., 960); but when further data were sought in reference to its precise habitat, there was found no reference to its discovery in the records of the laboratory of the Gardens, and a question existed in the mind of the pathologist as to the correctness of the label. There is therefore an uncertainty as to this specimen, which, however, if correctly labelled, is, as far as the writer knows, the first instance of its occurrence in the American bison.

62. *Filaria gracilis,* Rudolphi (Path. Hist., 1642, 1645), has been identified from specimens found in the peritoneal cavity of two monkeys in the Zoölogical Gardens, the first a white-throated cebus, *Cebus hypoleucus* (P. Z. G. Lab., 955), the second from an unindicated species.

63. *Filaria pungens,* A. Schneider (Path. Hist., 1696, 1716), is recorded as found in the air sacs of a red-headed weaver-bird, *Tondia madagascariensis* (P. Z. G. Lab., 1028), and from the peritoneum of a blue-bearded jay, *Cyanocorax cyanopogon* (P. Z. G. Lab., 404).

64. *Filaria australis,* Linstow (Path. Hist., 1701), was met in the peritoneal cavity of a brush-tailed wallaby, *Petrogale penicillata,* from the Zoölogical Gardens. The writer regards the specimen described as *Filaria spelæa,* Leidy (Pr. Acad. Nat. Sci., Phila., 1875, vol. 27, p. 17), as probably identical, in which case Leidy's name would take preference to that of Linstow's.

65. *Spiroptera incerta,* n. s. (Path. Hist., 1109, 1120, 1453, 1463, 1613, 1616, 1618, 1619, 1620, 1621, 1622, 1623, 1624, 1625, 1626, 1627, 1628, 1629, 1630, 1631, 1644, 1661, 1672, 1675, 1686), has been met in the proventricle and gizzard of several dozen birds. The parasite has been endemic in the bird house at the Zoölogical Gardens, and has appeared particularly among the parrakeets, amazons, conures, and parrots; but in the list there is also an instance of its occurrence in a valley quail, and quite recently (not included in the present list) it has appeared among the pigeons. For a description and fuller account of the various hosts, see special article in this journal (p. 291).

66. *Spiroptera* (?) *iguanæ,* n. s. (Path. Hist., 1641), from the lung of a Cuban iguana, *Cyclura nubila* (P. Z. G. Lab., 1127). For description, see special article in this journal (p. 293).

67. *Dispharagus ardeæ,* n. s. (Path. Hist., 1681), was met in the alimentary canal of a blue heron, *Ardea herodias* (P. Z. G. Lab., 1158). A single female specimen was found along with a number of ascarides (*Ascaris ardeæ, supra* 34) and fragments of *Tænia unilateralis* (*supra,* 16). The entire lot of material was submitted in one bottle, with the statement that the worms were found in the proventricle, stomach, and intestines of the bird, and it is impossible to fix the precise habitat in the canal for the specimen here listed. For description, see special article in this journal (p. 293).

68. *Anguillula aceti* (Path. Hist., 60). Dr. A. F. Coca, in examining a specimen of human urine submitted to the laboratory for diagnostic purposes, met numerous examples of anguillulæ in the fluid; but, inasmuch as the urine was contained in an old wine bottle, and subsequent specimens from the same patient, collected and preserved under careful precautions, showed none of the worms, it was assumed that the examples first observed had been present in acetous remnants in the bottle and were not to be regarded as one of the occasional instances of parasitism by this worm in the urinary or urogenital tract of man.

B. ARTHROPODA.

69. Larvæ of *Lucilia macellaria,* (Fabricius) (Path. Mus., 10), the common "screw-worms" of the South. The specimens were removed from an ulcerous wound (in which the ova of the fly had been deposited) upon the forehead of a girl in Galveston, Texas, by Dr. J. J. Terrill.

70. Larvæ of *Hypoderma lineatum,* (de Villers) (Path. Hist., 851), from the subcutaneous tissue of the face of a boy, aged three years, at Glasgow, Montana, a case of Drs. Hoyt

and Getty. The child had had a series of swellings located upon the face, thigh, and other parts of the body, dating back to October, 1905; these attaining the size of half of a small apple, each with the appearance at the apex of a small, bluish hemorrhagic point. After the appearance of this apical spot the swellings would diminish and disappear, to be succeeded by similar lesions elsewhere. Finally, in February, 1906, one developed on the face, in which, after it had been well poulticed, the dark spot broke and the single grub appeared, which was submitted for identification. The writer has on one other occasion met a similar occurrence of the larva of this fly in man, in a case of Dr. Herff, of San Antonio, Texas (*Med. News*, December 6, 1902). In neither of these cases was the grub in the last moult.

Here, too, should be listed examples (Path. Mus., 13) of the so-called *Hypoderma ovis* larvæ, collected by Dr. J. J. Repp from the subcutaneous tissue of a sheep, *Ovis aries*, in Iowa. The grubs met in sheep beneath the skin are generally held to be larvæ of *H. lineatum* rather than those of a separate species, as has often been supposed. These are considerably larger than the human specimens just mentioned, and probably represent a more advanced moult than the above.

71. Larvæ of *Cuterebra fontinella*, Clark (Path. Hist., 1798), obtained by Dr. R. C. Rosenberger from the subcutaneous tissue of the neck of a common cotton-tail rabbit, *Lepus sylvaticus*, killed in the vicinity of this city.

72. Larvæ of *Gastrophilus equi*, (Clark) (Path, Mus., 12), obtained by Dr. J. J. Repp, in Iowa, from the gastric mucous membrane of a horse, *Equus caballus*.

73. *Clothilla inquilina* (Path. Hist., 1064). These insects were sent through the Pennsylvania State Health Department to the laboratory by Dr. Koch, of Lyons Station, Penna., with the statement that they had infested in great numbers the clothing of one of his patients, a woman, and had caused an irritation similar to that produced by body lice. The same insects swarmed in a mill owned by the patient's husband. This insect has been met a number of times as an insect pest (cf. Railliet, Blanchard et al.). It is very similar to *Clothilla pulsatoria* (one of the "death-watch" insects), which Professor J. B. Smith, of Rutgers College, mentions in the New Jersey State Entomological Catalogue as closely resembling lice and being occasionally mistaken for them, and as sometimes taking practical possession of a whole house and becoming intolerable nuisances to the inhabitants. It is believed to be the same insect which Gay, in 1878, described as a parasite of horses under the name *Trichodectes quadricornis*.

74. *Boöphilus bovis*, Curtice (Path. Mus., 11), the common cattle tick, the carrier of Texas fever of cattle, collected in Iowa by Dr. J. J. Repp.

75. *Pentastoma denticulatum* (Path. Hist., 1640), the larval stage of *Linguatula rhinaria*, (Pilger), from the lung of a gazelle, *Gazella dorcas*, from the Zoölogical Gardens.

76. *Demodex folliculorum*, var. *hominis*, (Simon) (Path. Hist., 210), was encountered in the ducts of the sebaceous glands in a section of a chronic inflammatory lesion of the eyebrow of a woman in St. Mary's Hospital, Philadelphia, submitted for examination by Dr. J. M. Swan. The parasites are probably only coincident with the inflammation, but the inflammatory changes in the walls of the infested ducts suggest that they may have had some part in maintenance of the long-standing irritation producing the lesion.

PLATE I.

Oxyuris evoluta. Linstow: (camera lucida drawings; a line is drawn from each figure to the scale of enlargement employed).

FIG. 1.—Outline of complete worm: *a*, intestine; *b*, vaginal protrusion; *c*, intracorporeal portion of vaginal tube; *d*, d_1, d_2, uterine canal and its expanded portions; *e*, oviduct and ovarium; *f*, anus; *g*, esophagus and bulb; *h*, fusiform cuticular expansion at head end.

FIG. 2.—Frontal view of head end: a_1 dorsal lip; a_2, ventral lips; *b*, one of the three lip-like extensions of cuticle over the lips proper; *c*, one of the two dorsolateral cuticular swellings showing its three papillæ.

FIG. 3.—Lateral view of head end.

FIG. 4. Head end, showing esophagus and bulb: *a*, fusiform cuticular swelling; *b*, esophagus; *c*, esophageal bulb, with its armature.

FIG. 5. Transverse section of esophagus in its posterior portion, showing its triradiate lumen.

FIG. 6.—Details of genital apparatus: a_1 body wall; *b*, extracorporeal vaginal protrusion; *c*, intracorporeal portion of vagina; *d*, d_1, d_2, uterine canal with its cyst-like expansions; e_1, ovarium; e_2 e_3, oviduct plicated along uterus and entering posterior end of latter at e_3.

PLATE II.

Tænia paradoxuri and *Colugnia browni:* (camera lucida drawings; a line from each drawing indicates the scale of amplification employed).

FIG. 1.—*T. paradoxuri:* head and first links, showing the conical u armed rostellum, and the oval suckers with a curved slit-like orifice.

FIG. 2.—Frontal view of head of *T. paradoxuri.*

FIG. 3.—Outline of anterior segments (2 cm. from head) of *T. paradoxuri.*

FIG. 4.—Outline of segment of *T. paradoxuri* near posterior portion of strobile, showing the capacious genital pore.

FIG. 5.—Ovum of *T. paradoxuri.*

FIG. 6.—*C. browni:* frontal view of head, showing depressed rostellum surrounded by row of numerous small hooks, and the globose suckers with circular orifices.

FIG. 7.—Lateral view of head and anterior segments of *C. browni.*

FIG. 8.—Isolated hook from armature of head of *C. browni.*

FIG. 9.—Diagrammatic drawing of fully developed but non-gravid segment of *C. browni* at 8 cm. from head (constructed from sections and from compressed segments): *C*, cirrus; *T*, testicles; *RS*, receptaculum seminis; *Or*, ovary; *Vg*, vitelline gland; *Ut*, uterus.

FIG. 10.—Ovum of *C. browni.*

PLATE III.

Tænia cuncetes: (camera lucida drawings, except Fig. 4, which is diagrammatic in part, the general outlines, however, being from camera lucida tracings; the scale of enlargement employed is indicated by a line drawn from each drawing).

FIG. 1.—Head and incompletely grown strobile, without gravid links.

FIG. 2.—Frontal view of head.

FIG. 3.—Segments taken from a fully developed strobile from near head, to show the early development of the genital parts. (These were drawn by camera lucida from compressed links, which were originally considerably larger than the first links of the undeveloped strobile in Fig. 1, but which, by the compression, were much increased in both length and width).

FIG. 4.—Fully developed, but as yet non-gravid segment (partly diagrammatic); shows genital parts of segment: cirrus pouch, (*C*); genital pore, (*GP*); vagina, (*V*); receptaculum seminis, (*RS*); uterus, (*Ut*); testicles, (*T*); ovary, (*Or*), and vitelline gland, (*Vg*).

FIG. 5.—Ovum with surrounding amnion.

PLATE IV

Ascaris h ploptera, Rud., new variety: (camera lucida drawings; a line from each drawing indicates the scale of enlargement employed).

FIG. 1.—Two ova, the one to the right containing a larval worm.

FIG. 2.—Anterior end of worm, to show extent and shape of alar cuticular expansions (*a*).

FIG. 3.—Internal aspect of dorsal lip, showing denticulate border and lobes of pulpa: *a*, denticulate border of lip; *b*, outer paired lobe; *c*, inner paired lobe; *d*, unpaired lobe.

FIG. 4.—External view of head from ventral surface, showing the two ventral lips with their papillæ; on either side the first part of alar cuticular expansion.

FIG. 5.—Anterior view of head, showing lips and papillæ (dorsal lip above), and beginnings of cuticular expansions laterally.

FIG. 6.—Ventral surface of tail of male; the cuticle, having been cut on the dorsum, is seen spread out laterally; shows the details of the postcloacal papillæ: *c*, cloaca.

FIG. 7.—Lateral view of tail of male, showing both postcloacal and precloacal papillæ: *c*, cloaca.

FIG. 8.—Tail of female; *a*, anus.

PLATE V.

Ascaris aquilæ: (camera lucida drawings).

FIG. 1.—Inner aspect of dorsal lip: *A*, interlabium, *B*, lobus impar; *C*, inner paired lobe; *D*, outer paired lobe. (Same scale of enlargement as Fig. 2.)

FIG. 2.—Outer aspect of dorsal lip, showing papillæ, and the deep incision in anterior margin.

FIG. 3.—Frontal aspect of head, showing the lips and interlabia and the papillæ of the lips.

FIG. 4.—Lateral aspect of head.

FIG. 5.—Ovum, drawn to show in upper part the tuberculated outer surface of the shell, and in the lower part the segmented interior.

PLATE VI.

Ascaris ardeæ (camera lucida drawings; scale of enlargement is indicated by a line from each drawing).

FIG. 1.—Lateral view of anterior end, showing two of the lips (partly in profile) and two of the interlabia.

FIG. 2.—Frontal view of the head, showing the dorsal lip below and to the left.

FIG. 3.—Internal aspect of dorsal lip and two interlabia, showing details of pulpa of lip.

FIG. 4.—Tail of female.

FIG. 5.—Ovum, above showing the pitted external surface of the shell, and below showing the segmented interior.

FIG. 6.—Ventral surface of male tail. (Note the second pair of papillæ from tip of tail as uncertain.)

FIG. 7.—Lateral view of tail of male.

PLATE VII.

Oxyuris microtyphlon and *Oxyuris megatyphlon:* (camera lucida drawings; scale of enlargement is indicated for each by a line).

FIG. 1.—Ovum of *O. microtyphlon.*

FIG. 2.—Ovum of *O. megatyphlon* (same scale, drawn in outline for comparison).

FIG. 3.—Frontal view of head of *O. microtyphlon,* showing the three lips and their papillæ.

FIG. 4.—Ventral view of tail of male of *O. microtyphlon* (to the left at the tip of the tail is a lateral view of the same for comparison; dotted lines connect identical structures): *a,* cuticle, showing the transverse striations; *b,* intestine; *c,* anterior lip of cloaca; *d,* posterior lip of same; *e,* postcloacal papillæ; *f,* postcloacal spinous support of tip of tail, bidigitate at its free end; *g,* larger intraeuticular spine in tip of tail; *h,* spicule; *i,* body cavity.

FIG. 5.—Female example of *O. microtyphlon: a,* anus; *v,* vulva; *o,* ova in uterine canal; *b,* esophageal bulb; *e,* esophagus. The length of the specimen has been indicated by lines drawn into the body of the worm at intervals of 1 mm. from the head posteriorly.

FIG. 6.—Tail of a non-gravid female, showing the closer relation between the anus (*a*) and vulva (*v*) than in the preceding.

FIG. 7.—Male specimen of *O. microtyphlon* (same enlargement as Fig. 5, for comparison of size of male and female): *e,* esophagus; *b,* bulb of esophagus; *i,* intestine; *s,* spicule. (Length marked at millimeter intervals from head posteriorly.)

FIG. 8.—Tail of male *O. microtyphlon* with spicule partly protruded: *i,* intestine; *s,* spicule.

FIG. 9.—Tracing of tail of male *O. megatyphlon* from Schneider.

FIG. 10.—Tail of male *O. megatyphlon* from author's material.

FIG. 11.—Tail of female *O. megatyphlon* (author's material), showing relative position of anus (*a*) and vulva (*v*).

FIG. 12.—Head end of *O. megatyphlon* (author's material).

PLATE VIII.

Globocephalus ardeæ: (camera lucida drawings; scale of enlargement indicated for each drawing by a line).

FIG. 1.—Frontal view of head showing mosaic appearance, the mouth and its chitinous ring and intra-oral spines (?), and showing faintly the armature at the base of the mouth cavity.

FIG. 2.—Armature of three curved chitinous plates (*a*) set in the floor of the mouth about the esophageal opening (*c*), and the three-sided chitinous ring (*b*) about the esophageal orifice.

FIG. 3.—Head end, showing (*a*), mouth; (*b*), mouth cavity; and (*c*), armature; (*d*), esophagus and cervical papillæ (*e*); and the cuticular collar (*f*) about the head and first part of neck.

FIG. 4.—Tail of female, showing (*a*) anus and (*b*) vulva.

FIG. 5.—Ova.

PLATE IX.

Spiroptera incerta: (camera lucida drawings; the scale of enlargement is indicated for each drawing by a line).

FIG. 1.—Low amplification of a female worm, showing position of vulva (*V*), the divisions of the esophagus (*O*), position of anus (*A*), and the intestine (*I*).

FIG. 2.—Head end, showing cuticular expansions.

FIG. 3.—Transverse section of anterior end, showing cuticular expansions.

FIG. 4.—Frontal view of head, showing (*a*), lateral toothed lips; (*b*), dorsolateral, and (*c*), ventrolateral (submedian) lips; (*e* and *f*), dorsal and ventral tooth-like structure; and (*g*), outline of oral orifice.

FIG. 5.—Longitudinal view of head end, showing (*a*), lateral lip; (*b* and *c*), submedian lips; (*c*), median dorsal or ventral tooth-like structure; (*f*), mouth cavity; (*g*), first part of esophagus; (*h*), body wall; and (*i*), lateral cuticular expansions.

FIG. 6.—Outline of tail of female to show position of anus.

FIG. 7.—Ova, showing enclosed larvæ.

FIG. 8.—Ventral view of tail of male, showing (*a*), cuticular striations of the general body; (*b*), the quadrilateral cuticular plates within bursa; (*c*), cuticular expansions forming the bursa; (*d*), cloaca; (*e*), spicules, and the papillæ of the tail.

FIG. 9.—Specially enlarged view of the ventral side of tip of tail to show the small papillæ of this portion.

PLATE X.

Spiroptera (?) *iguanæ* and *Dispharagus ardeæ:* (camera lucida drawings; scale of enlargement indicated by line drawn from each figure).

FIG. 1.—*Spiroptera* (?) *iguanæ:* ventral surface of tail of male, showing tip of tail and arrangement of papillæ about the cloaca.

FIG. 2.—*Spiroptera* (?) *iguanæ:* lateral view of tail of male, showing (*a* and a_1), the principal and accessory spicules and (*b*) the cloaca.

FIG. 3.—*Spiroptera* (?) *iguanæ:* head end, showing (*a*), mouth and (*b*), esophagus (structure of lips uncertain).

FIG. 4.—*Dispharagus ardeæ:* anterior end viewed laterally, showing (*a*), one of the lateral lips; (*b*), the "cordons;" (*c*), the anterior narrow, and (*d*), posterior wider portions of the esophagus.

FIG. 5.—*Dispharagus ardeæ:* frontal view of head (lips bent to one side by pressure of coverglass), showing (*a*), the two lateral lips and (*b*) the beginnings of the lateral cords at bases of lips. (Scale of enlargement below, same as for Figs. 4 and 6.)

FIG. 6.—*Dispharagus ardeæ:* tail of female, showing position of anus (*a*), and the mammillary eminences (*b*) alongside of anus.

PLATE I

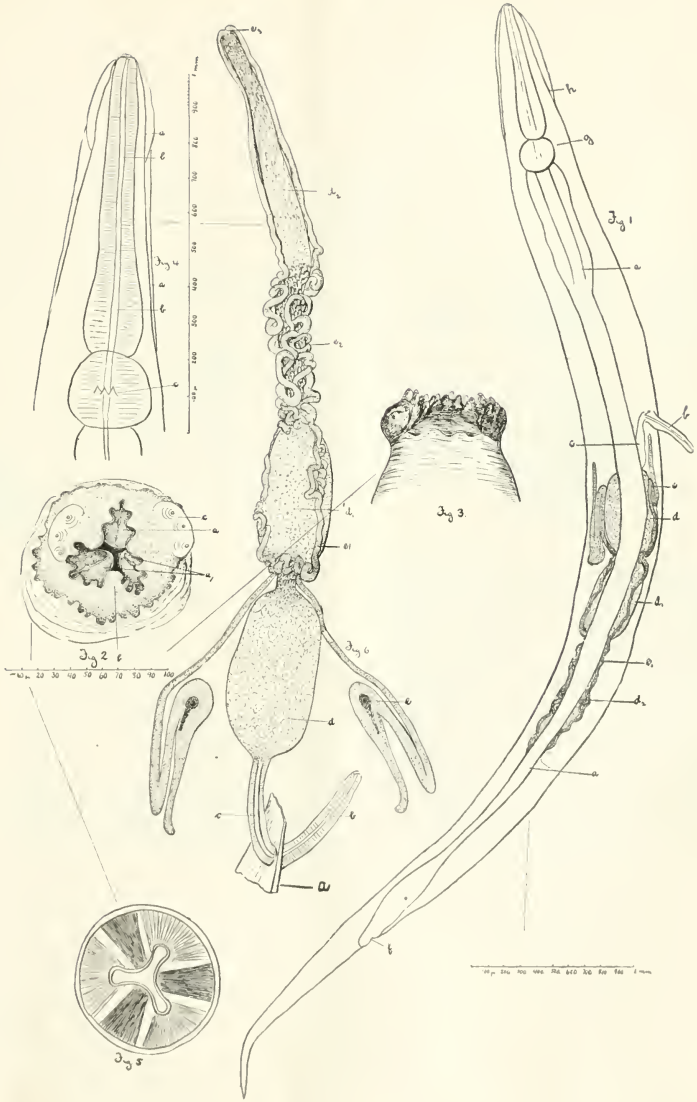
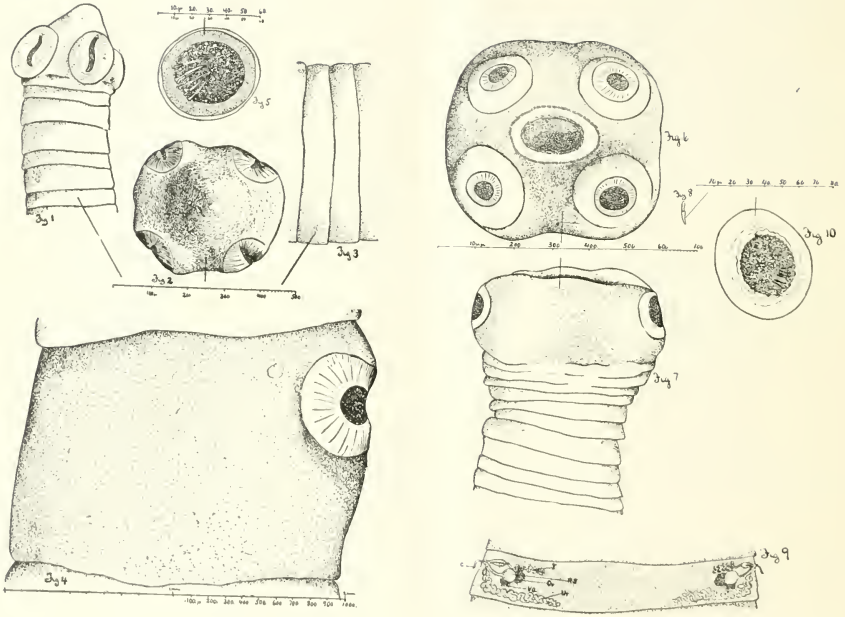


PLATE II



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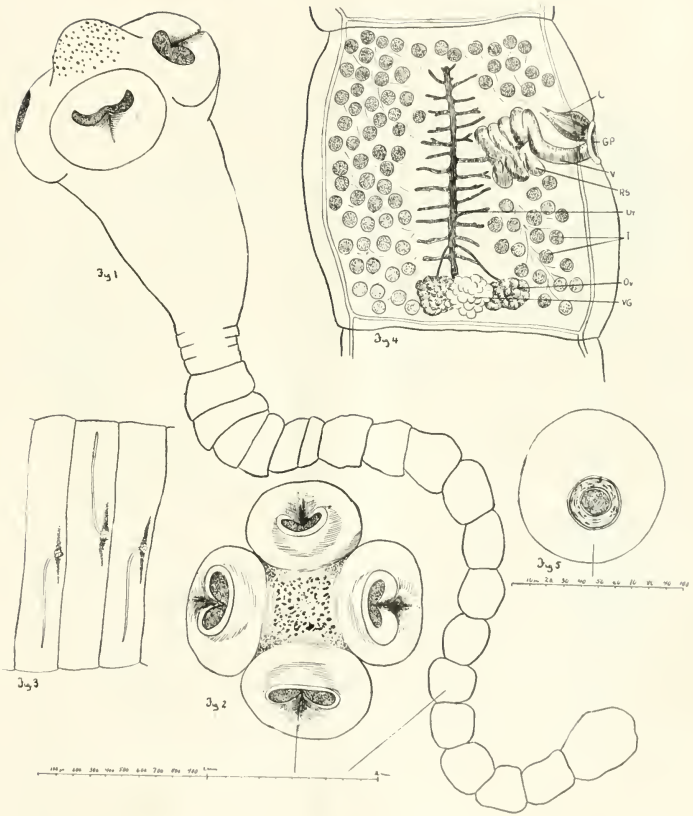


PLATE IV

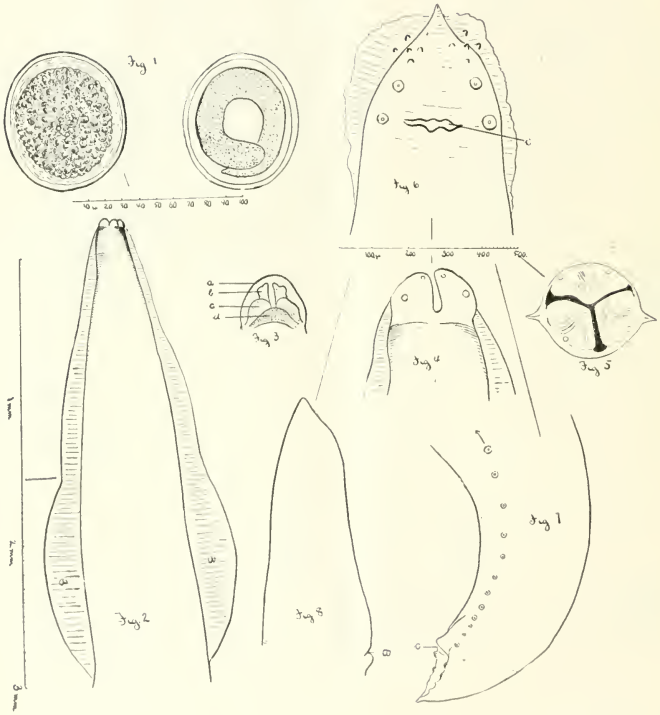
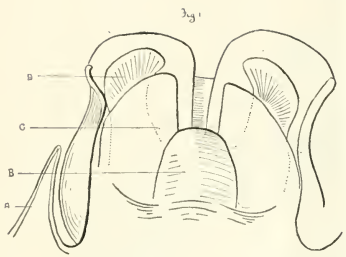
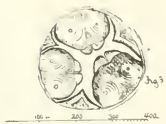
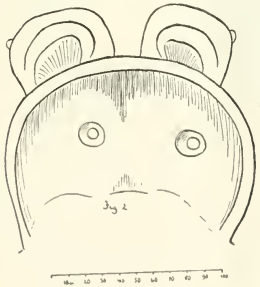


PLATE V







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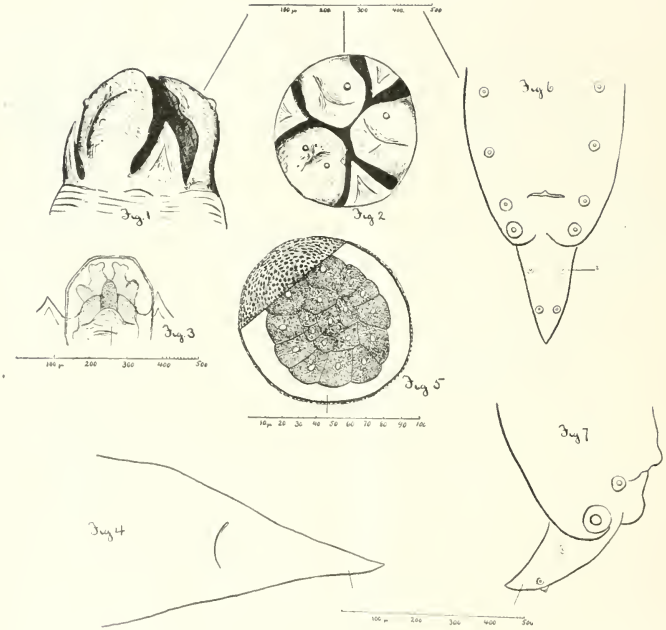
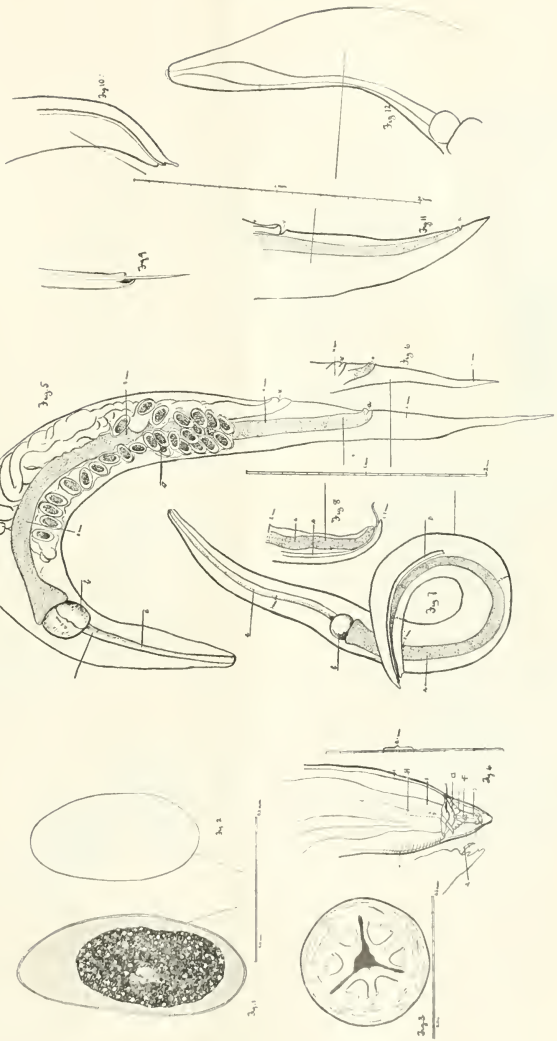


PLATE VII



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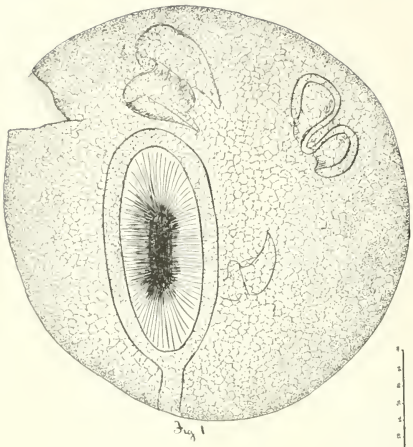


Fig 1

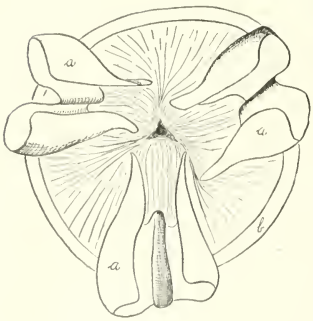
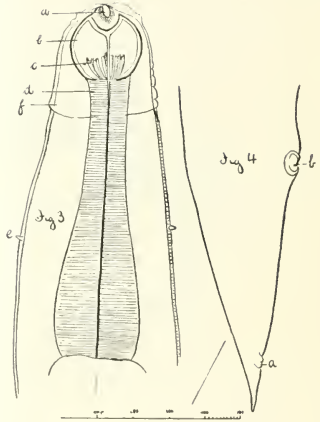


Fig 2



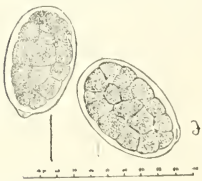


Fig 5

PLATE IX

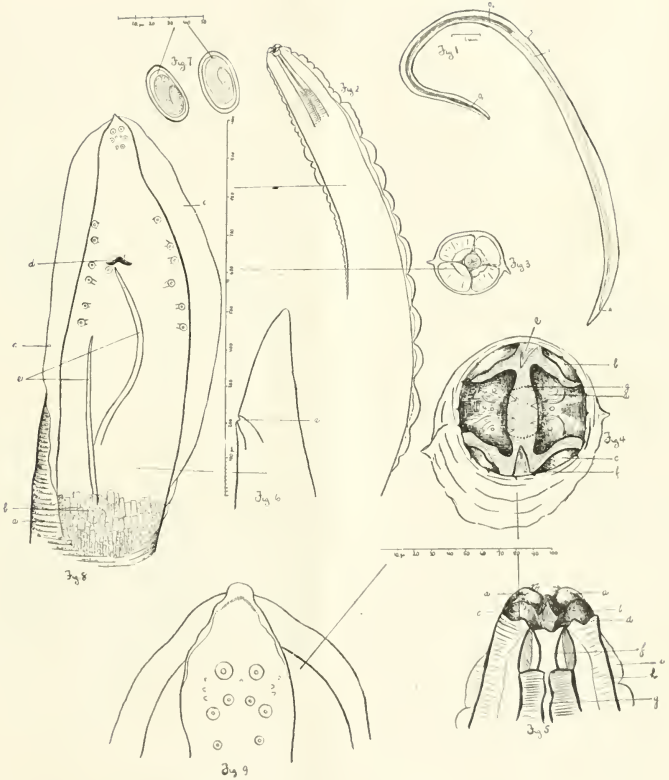
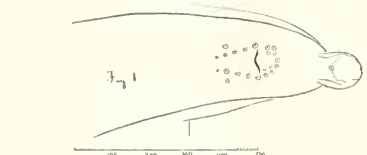
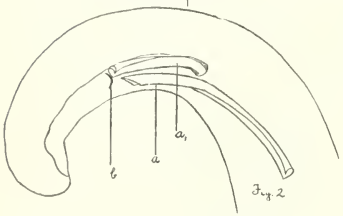
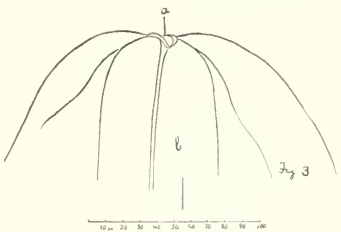
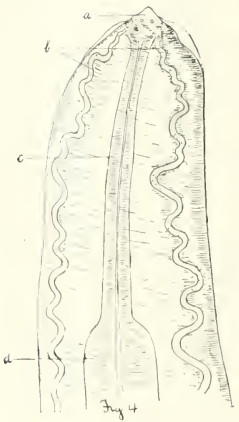


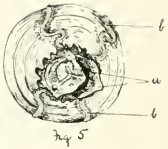
PLATE X

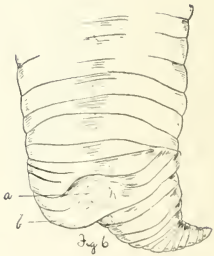












CONTRIBUTIONS TO SYSTEMATIC HELMINTHOLOGY.

By Allen J. Smith, M.D., Herbert Fox, M.D., and C. Y. White, M.D.

(From the McManes Laboratory of Pathology of University of Pennsylvania and Laboratory of Comparative Pathology of the Philadelphia Zoological Gardens.)

The following notes of identification, believed to concern for the most part new helminthological species, have been made in the course of study of the parasites enumerated in the synoptic article upon parasites in this journal in the pathological laboratory of the University of Pennsylvania. The specimens upon which the descriptions are based have been obtained for the most part from animals of the collection of the Philadelphia Zoölogical Gardens which came to autopsy in the laboratory of the Gardens at the hands of Drs. Fox and White, who transmitted them for identification to the first-named writer. While most are new species, at least one has been included which has been previously known, but is here considered because it seems to present special variations.

In all cases where the material permits, types of these parasites will be placed in the collection of the Academy of Natural Sciences in Philadelphia, as well as in the Pathological Museum of the University of Pennsylvania.

Tænia paradoxuri, n. s. (Plate II, Figs. 1 to 5).

The material (No. 14 of Synopsis, this journal; Path. Hist., 1714) in this instance was obtained from the dejecta of a living animal, a Gray's paradoxure, *Paradoxurus grayi* (habitat, India), and includes one well-developed strobile of the tapeworm together with fragments of several more, one of these fragments consisting of a second head and some of its anterior segments. All of the material was unfavorable for study, both because of the close adherence of extraneous (fecal) matter, which it was impossible to safely dislodge either by mechanical means or by various solvents employed, and because the tissue of the worms was more or less disintegrated when received and poorly adapted to section and staining methods of study.

The complete strobile measures 160 mm. in length, and is made up of over three hundred segments. It attains its greatest width in the level between 120 and 140 mm. from the head, where the links (Fig. 4) are 3 mm. wide and 1 mm. long; thence posteriorly it narrows to a terminal link slightly more than 1 mm. wide and 2 mm. long. The anterior links (Fig. 3) are decidedly wide in proportion to their length, measuring at 20 mm. from the head 0.15 mm. wide and 0.04 to 0.06 mm. long. There is no neck, the first segment being clearly outlined immediately back of the head, being 0.25 mm. wide and 0.03 mm. long. Viewed laterally the head (Fig. 1) is slightly wider than the first segments, and is provided with four suckers and a low, broadly conical, retractile rostellum devoid of armature. The retractile character of the rostellum is inferred from the fact that in one of the heads the frontal region between the suckers was practically flat, while in the other the conical appearance described was definitely present. Viewed from the front (Fig. 2) the outline of the head is a quadrilateral, with the dorsoventral diameter slightly greater than the lateral (dorsoventral, 0.35 mm.; lateral, 0.25 mm.). The suckers are prominent, oval in shape, with their long axes in the long axis of the strobile; and open by a curved, slit-like orifice extending in the longitudinal direction of the worm. Suckers measure 0.15 by 0.13 mm.

Genital pores (Fig. 4) marginal, irregularly alternating; marked by very large orifices and prominent lips; are situated toward the anterior part of the margin of the link. Ova (Fig. 5) spheroidal, with thin, smooth, colorless external wall (outer diameter 55 to 60 micromillimeters), enclosing a colorless, finely granular albuminous layer; within the latter a yellowish embryophore, 40 mm. in diameter, coarsely granular, hexacanthous. Embryonal hooklets measure 18 to 20 micromillimeters in length.

Tænia eunectes, n. s. (Plate III).

In the small intestine of an anaconda, *Eunectes murinus* (P. Z. G. Lab., 939), there were encountered seven small cestodes, apparently entire, together with a half-dozen undeveloped strobiles and several fragments of other strobiles of the same parasite (Path. Hist., 1694; No. 15, Synopsis, this journal). The largest of the entire strobiles measured between 9.5 and 10 cm. in length and was made up of between two and three hundred proglottides. The worm reaches its greatest width of segments at about 7 cm. from the head, where it is 2 mm. in width. All the larger specimens were marked at various positions with one or more knot-like swellings (probably due to contraction of the worm in life). The head (Fig. 2) viewed from the front presents a crucial appearance from the prominence of the suckers, measuring transversely across two opposed suckers 1.5 mm. and laterally across two adjacent suckers 1.3 mm. The transverse diameter of the square front between opposed suckers measures 0.4 mm. The suckers, thus prominent, form the rounded arms of the crucial frontal picture, each sucker being globose

in shape and having a lateral diameter of about 0.7 mm. The orifice of each sucker is a rather wide slit, running laterally; and as a peculiarity, common to all the heads included in the material obtained, the outer wall of each sucker is depressed and its margin turned in, forming an angular intrusion into the cavity of the sucker. The central part of the front of the head, between the suckers, forms a broad and low cone (Fig. 1); and is unarmed in all the specimens, but the cuticle here contains numerous small, granular, non-polarizing bodies, which in life probably projected slightly above the surface to give it a slight roughness. Back of the suckers the head is prolonged as an inverted truncated cone for a little over 0.1 mm., narrowing from 0.9 mm. at the level just behind the suckers to somewhat over 0.3 mm. in width at the posterior portion where the segments begin (the level of truncation of the inverted cone).

In the young and incompletely formed strobiles (Fig. 1) the proglottides are all small, those next the head somewhat broader than long, but soon becoming square to ovoid in outline and more loosely attached to each other (moniliform) than is seen in any part of the adult strobiles. These seem all to be neuters, and, judging from their shape and appearance, never become developed, and are pushed along in the growth of the strobile by the formation of efficient links as the head becomes older. In the fully developed strobiles the neck segments are at first about a millimeter wide (wider than the terminal part of head) and 0.1 mm. long; in their fullest development (at widest part of strobile) they remain somewhat wider than long (2 mm. wide and 1 to 1.8 mm. long); thence to the end they diminish in width, becoming square and finally longer than broad (1.5 to 1.8 mm. long and 1 mm. or less in width). The links in these fully formed specimens are not sharply defined from each other, the anterior margins of a given proglottis being of almost the same width as the posterior margin of its predecessor, thus not permitting much overlapping of the former by the latter. Without staining the lines of separation between the proglottides are inconspicuous, the first impression being of a continuous surface. One of the surfaces of the larger links is usually somewhat convex, the opposite side showing a longitudinal concave depression along the middle of the link. Genital pores irregularly alternate. The uterus in efficient but as yet non-ovigerous links (Fig. 4) shows as a median longitudinal tube, with about a dozen lateral branches extending toward the margins of the link, these when filled with ova showing as thick, round-ended, club-like branches. The two ovaries and vitelline gland lie along the posterior margin of the link, much as in *Tænia saginata*, the vitelline gland directly back of the uterine tube, the ovaries spreading out on either side, their oviducts joining the uterine canal a little in front of its posterior end. Between the uterus and the genital pore there is a thick plicated tube, regarded by the writers as a receptaculum seminis. The cirrus is slender; cirrus pouch thick and muscular; the testes in non-gravid links numerously seen in the lateral fields.

The ova (Fig. 5), when obtained without tearing it, show a delicate colorless outer sac (amnion?), within which lies the ovum proper; this sac is spheroidal and measures 85 to 90 micromillimeters in diameter. The ovum is spherical, double walled, colorless, with a coarsely granular and somewhat laminated material between the walls; the enclosed embryo granular and provided with six hooklets. Outer diameter of ovum, 28 to 30 micromillimeters; diameter of embryophore, 16 to 18 micromillimeters.

Examination of helminthological literature at command of the writers has thus far failed to show any tænia having comparable features to the above, and for this reason it is believed to constitute a new species, for which the name *Tænia eunectes* is proposed.

Cotugnia browni, n. s. (Plate II, Figs. 6 to 10).

From the tapeworms of the type of the dipylidium group, with two sets of genital organs in each segment, the genus *Cotugnia* was framed to include those cestodes having such arrangement of the genital apparatus met in birds and provided with a rostellar armature of numerous hooklets, by Diamare (*Boll. soc. di naturalisti in Napoli*, 1893, ser. i, vol. vii, p. 10), with *C. digonopora* of fowls as the type. The following specimens (Path. Hist., 1672) are believed by the writers to constitute a new species of this genus, to which provisionally they would assign the name *Cotugnia browni*.[1] The material was obtained at autopsy from the intestine of a banded parrakeet, *Palavornis fasciatus* (P. Z. G. Lab., 1052), along with a number of specimens of *Spiroptera incerta*, n. s. There were included four strobiles, the largest 140 mm. in length and apparently entire; two two-thirds to three-fourths the length of the first and lacking the terminal links; and the fourth only 5 cm. long and possessing no ripe segments. In addition there were several fragments made up of ripe links, evidently broken from one or other of the shorter strobiles. The largest example attained its greatest width 100 mm. from the head, where the segments were 4 mm. wide, diminishing thence posteriorly, so that the terminal links were but 3.5 mm. in width. The strobile included a few more than two hundred segments. The head was small and short, with quadrate front (Figs. 6 and 7); measured 0.3 mm. in length, and over the front dorsoventrally 0.55 mm., laterally 0.6 mm. Four prominent suckers, globose in shape, with full diameter of 0.2 mm., and circular orifice 0.05 mm. in diameter; suckers unarmed. Rostellum of all the heads depressed, provided with a circle (Figs. 6 and 8) of numerous (over two hundred)

[1] Named for Dr. Arthur Erwin Brown, Secretary of Philadelphia Zoological Society.

small hooklets (0.012 to 0.014 mm. in length). Neck short. First links (Fig. 7) much wider than long (0.4 mm. wide, 0.03 to 0.05 mm. long); immature links showing the developing genital organs (60 to 80 mm. from head) from 2.5 to 3 mm. wide and 0.5 to 1 mm. long; largest ripe links (100 to 110 mm. from head), 4 mm. wide and 1.5 mm. long; terminal links, 3.5 mm. wide and 1.5 mm. long. Double genital apparatus (Fig. 9); a genital pore on each lateral margin of link at first third of its length, the cirrus usually protruded for 0.1 or 0.2 mm., smooth, with slightly curved end. Cirrus pouch thick and flask-shaped, anterior; a half-dozen or more small testes in anterior portion of link, sessile upon the vas deferens. Vagina thick-walled, opening into a spheroidal receptaculum seminis about midway between anterior and posterior margins of link and external to testes; ovary rosette-shaped and lying to median side of receptaculum; vitelline gland posterior to receptaculum. Uterine tube, with egg sacs, extends along the posterior margin of link toward median line, the tubes of the two sides not meeting. In ripe links the uterine tubes fill nearly the entire link, the ova being held in the reticulately distributed tubes and freed therefrom with difficulty on tearing the segments, each being held by some surrounding adherent material. Ova (Fig. 10) colorless, spheroidal, with a thin, pliant outer membrane, within which is a granular and slightly laminated material separating the outer membrane from the embryo. The latter has no distinct membrane separating it from the surrounding granular matter, is yellowish in hue, hexacanthous, coarsely granular, and its outer surface rough with irregular elevations. Outer wall of ovum measures 66 to 70 micromillimeters in length by 56 to 60 micromillimeters transversely.

Ascaris leptoptera, Rudolphi (*ex parte*), new variety (Plate IV).

The ascarides of the larger members of the cat family have been the source of no little confusion from the first in the endeavor to separate them from the common *Ascaris canis* (Werner) of the cat and dog; and there is little constancy of description of the ascarides derived from lions alone, not to speak of the differences announced between those of lions, tigers, and other of these larger cats. Rudolphi (*Entozoa*, II, i, p. 140) created a new species of the group for an ascaris from a lion in the Zoölogical Gardens of Leipsic, the verity of which has at one time been affirmed and again denied by nearly every writer since then. Much stress was originally laid upon the precise appearance of the alar cuticular expansions, and probably much of the confusion has arisen from the apparent fact that these are by no means constant in size and shape, and seem to be at times entirely absent. That there are several closely allied species, and that there may be a number of more or less distinct variations, can scarcely be denied, and until breeding experiments are added to the existing morphological observations it is not likely that the difficulties of classification will be entirely removed.

To illustrate the confused status of the question, these outlined descriptions may be here quoted. Schneider (*Nematoden*, p. 39; Pl. I, Fig. 5), accepting Rudolphi's specific name, *Ascaris leptoptera*, but declaring that his original specimens were but *Ascaris canis* (Werner), describes, from material including several hundred specimens from a lion born in London and examined after death at nineteen months of age in Berlin, a parasite having the following characteristics: Females, 65 mm. long; males, 46 mm. long. Lips equal, digitate, with rather pointed anterior margin and broader base. Denticulation poorly developed and inconspicuous, only showing along the lateral borders. Lobes of pulpa of dorsal lip long, undivided. Lateral alar membranes extend from head 4 mm. posteriorly, rounded at posterior termination. The head, even in the youngest examples, is deeply retracted between the salient cuticular expansions. Vulva 25 mm. from anterior end of worm. Shell of ovum thick, unmarked or only with irregular, trabecular reticulation. Tail of male lancet-shaped, slightly broadened, and with the ventral side flattened. Thirty-five pairs of papillæ, six postanal, the terminal and adjacent ones with conical base; the rest all raised, with pointed tips; all in uniform row.

Chatin (*Mém. de la Soc. de Biol.*, 1877, p. 266) records from a lion a number of ascarides without alar cuticular expansions, buccal lobes deeply divided, straight esophagus with ventricle (bulb); males reaching 25 mm. in length and having long double genital spicules; females attaining a maximum length of 80 mm. and with the vulva anterior to the first third of the body length. Ova 0.08 mm. (stated by Chatin 0.8 mm.—evidently a mistake) in length and 0.074 mm. transversely, without reticulation of the shell. For this material the author argues identity with Rudolphi's original *Ascaris leptoptera*.

On the other hand, Linstow (*Arch. mik. Anat.*, lx, p. 217; Pl. XII, Fig. 1) differentiates from *Ascaris canis* (Werner) and *Ascaris leptoptera*, Rud., an allied species, under the name *Ascaris leonis*, having the following characteristics: Lips with rather broad base, finely denticulated borders, without interlabia. Dorsal lip broader than long, anteriorly rounded, its papillæ relatively posteriorly situated; pulpa with two lobules projecting anteriorly, each showing two rounded anterior prolongations. A lateral alar expansion on each side of head, attaining a width of 0.18 mm. anteriorly and diminishing gradually and uniformly as it extends backward (those of *A. canis* and *A. leptoptera* are narrow anteriorly and increase in width posteriorly to reach the body wall in their posterior positions by a sharp and almost rectangular curve). Males attain a length of 34 mm. and a thickness of 0.99 mm.; esophagus 1: 12 of body length;

male tail acutely conical, with small digitate tip; the feebly developed, small genital spicules, 0.83 mm. in length; 21 pre-anal and 4 postanal papillae in uniform lines, the anterior ones 3.04 mm. in front of tip of tail. Females attain 53 mm. in length and 1.38 mm. in thickness; caudal end lanceolate; vulva at 5.8 of body length. Ova with thick, smooth shell, without markings; ova measure 0.086 mm. long and 0.062 mm. in transverse diameter, and (a rare feature in genus *Ascaris*) contain a fully developed larval worm.

In the material from the Philadelphia Zoölogical Gardens there were included ascarides from two lions. At autopsy of the first (P. Z. G. Lab., 794), a lioness about ten years of age and a resident of the Gardens for nine years, dead from acute peritonitis following puncture of the intestinal wall by a spicule of bone, 36 specimens (Path. Hist., 1102), of which 23 were females and 12 males, with one badly damaged example undetermined, were obtained from the stomach and intestines. In addition to these a single male specimen (Path. Hist., 1148) was subsequently submitted, having been passed in the dejecta of a lion now living in the collection. On examination it was found to present precise identity with the first examples. The following notes of description were made from the study of the specimens from the first animal: There is considerable variation in size from age and state of development. The largest female measures 76 mm. in length; the largest male 62 mm. Worms cylindrical in section, with thickest level near middle of body length; and taper delicately anteriorly and posteriorly. Preserved specimens colorless (but with a reddish tinge in some, especially toward the posterior extremity, suggesting that in life they were of reddish hue), rigid. In both sexes the head end is inflexed. Cuticle finely striated transversely, expanded at head end into a semilanceolate alar extension (Fig. 2, *a*), beginning anteriorly close to base of lips and in the larger specimens extending posteriorly 3 mm., its widest portion at about its posterior fourth, where it attains a width of nearly 0.3 mm., its free border from this level to its coalescence with the body cuticle becoming thick and somewhat rounded (not as large or as cordate in outline as the wings of *Ascaris canis*, and not crenulate). Mouth terminal, provided with three nearly equal lips, the dorsal lip a little wider than the others (base of dorsal lip, 0.16 mm. transversely; of inferior lips, 0.13 mm). Diameter of face of cephalic end, 0.25 mm. Each lip bears two papillae on external surface. Dorsal lip broader than long (0.12 mm. from base to anterior border; base, 0.16 mm. transversely); anterior border convex and poorly defined from lateral borders, which are also convex. Poorly marked denticulation along both anterior and lateral borders (somewhat variable in the clearness of denticulation in different individuals). Pulpa (Fig. 3) shows an unpaired median lobe arising from base for one-third the length of lip; the paired lobes lobulate (anterior and lateral, each broad and subdivided as in drawing). Saddle-groove fairly deep. Inferior lips narrower and more digitate (Fig. 4), and more closely following Schneider's description for dorsal lip (*Nematoden*, Berlin, 1866, p. 39).

Tail of male (Fig. 7) incurved or often tightly enrolled, without cuticular expansions, terminating in a short cone (as wide at level of cloaca as it is long from this level), ending in a small cuticular spicule. Cloaca 0.18 mm. from tip of tail. Ventral surface of tail of male slightly flattened. Twenty-seven pairs of caudal papillae (Fig. 6), of which 7 are postcloacal. Of the postcloacal, 3 are lateral, small and conical, and likely to be overlooked, near the end of the tail; Nos. 4 and 5 are also small conical ones, at border of flattened ventral surface; Nos. 6 and 7 and all the precloacal papillae appear as small tips set upon a rounded eminence. They gradually increase in size anteriorly and are set in a regular row, succeeding Nos. 4 and 5 along the margin of the flattened ventral surface of tail. Spicules of male equal, small.

Tail of female (Fig. 8) a slender cone more than twice as long as the transverse diameter at level of anus; anus 0.7 mm. from tip. Tail straight or occasionally lightly enrolled. Vulva 5 m. from anterior end (length of worm used for measurement, 7.4 cm.); vagina short, dividing into two uterine canals with long plicated ovarian tubes, ranging posteriorly and anteriorly (anterior to vulvar level). Ova nearly spherical to oval in shape, smooth externally, and without markings on shell, thick-shelled, containing larvæ, measuring from 65 to 80 micromillimeters in diameter for the spheroidal examples, and for the oval ones from 75 to 85 in length and from 55 to 75 micromillimeters transversely (one very large example out of several hundred observed measured 105 by 55 micromillimeters). The ova here described were taken from the uterine tube of a damaged female, the genital tubes and intestine being protruded through the broken body wall and hanging freely exposed in the 4 per cent. solution of formaldehyde used as a preservative for twelve days before the study was made. Nevertheless, in many of the ova active vermicular movements persisted in the enclosed larval worms.

From comparison of the above data with the descriptions quoted in the early part of the article it is clear that the present specimens are to be classified as an intermediate variety between *Ascaris leptoptera* and Linstow's *Ascaris leonis*. Whether, in view of the marked variations which seem possible in these leonine ascarides, it is justifiable on purely morphological grounds to accept their specific separation is of course an open question; and to the writer it seems doubtful whether the matter can be determined short of careful feeding experiments. It is true the specimens here described seem more nearly related with Linstow's *Ascaris*

leonis than with *Ascaris leptoptera*, Rud., as described by Schneider; but in view of the existing uncertainty it has seemed best to adhere tentatively to the older specific name and relate our specimens as a variation thereof.

Ascaris aquillæ, n. s. (Plate V).

There were obtained from the proventricle of an American bald eagle, *Haliætus leucocephalus* (P. Z. G. Lab., 959), two nematode worms (Path. Hist., 1637; No. 32, Synopsis, this journal) at autopsy. Both were females and one was badly damaged, the head lost and the esophagus protruding from the broken end. It is stated that in addition to these specimens from the proventricle, larval filarial worms had in life been found in the blood of this worm, but at autopsy no adult filariæ were encountered.

The following description is based upon a study of the single perfect specimen. The worm is cylindrical in section, 50 mm. in length and 1.5 mm. in diameter at its thickest level (in third fourth of the body length), tapering anteriorly gradually to a rather bluntly rounded head 0.25 mm. in diameter at base of lips, and tapering posteriorly more rapidly to terminate in a straight, acutely conical tail. When received the specimens were colorless, with brownish lines of the intestine showing through the relatively opaque and thick body walls. Cuticle transversely striated; no alar expansions or other cuticular peculiarity. There are three thick and prominent lips (Fig. 3), each with two papillæ; well-marked interlabia. Lips free from denticulation, nearly symmetrical and equal. Dorsal lip (Figs. 1 and 2) four-sided, the anterior border deeply divided; groove of saddle deep and prolonged well to base. Anterior border projecting well beyond the pulpa on each side of saddle (like a finger-nail), its anterolateral angles auriculate (the lateral border being infolded and causing the angle to project slightly forward and laterally). Lateral border a double curve, concave anteriorly and convex posteriorly; apparently the entire margin infolded. Base about equal to anterior border of lip. Median unpaired lobe of pulpa extends from base about halfway to anterior margin of lip; two paired lobes, the inner large, its inner border straight and parallel with saddle-groove, its outer border broadly rounded to the tip, which is directed forward and slightly medianly. The outer lobule, more slender, extends further anteriorly, is undivided, and is directed anteriorly and toward the median line. Interlabia large, the margins infolded. Width of dorsal lip at base, 150 micromillimeters; width of anterior margin, 140 micromillimeters, distance from base to anterior margin, 110 micromillimeters. Esophagus long and slender, provided with a small and inconspicuous bulb at its posterior end, this latter with a posteriorly directed, finger-like diverticulum. Intestine at its beginning provided with a large, anteriorly directed, cecum-like diverticulum. Intestine and esophagus brown. Intestine large, straight, with numerous irregularities (like the haustra of the human colon), terminating at subterminal anus. Vulva small, inconspicuous, anterior to middle of body length. Vagina long, slender, muscular, opening into a capacious uterine canal with thin walls, which soon divides into two uterine tubes. Ovarian tubes very long and plicated tortuously about uterus and intestine. The ova (Fig. 5) are very variable in appearance (taken from both specimens). The best examples are elliptical to ovate in shape, with a thin, colorless, pliant shell-membrane, the external surface of which is thickly beset with small tubercle-like projections; the interior yellowish and coarsely granular, often segmented, and many examples containing larval worm met. They range from 80 to 90 micromillimeters in length and from 50 to 60 micromillimeters in width (one very large example measuring 100 by 70 micromillimeters was seen). In the absence of the male no full description is possible, but the above features are, as far as the writers at present know, unique. The parasite approaches *Ascaris spiculigera*, Rudolphi, and *Ascaris nasuta*, Schneider, both from pelicans and similar birds, and *Ascaris granulosa*, Schneider, from *Tachypetes aquilus;* but differs sufficiently in the details of the lip structure to permit specific differentiation.

Ascaris ardeæ, n. s. (Plate VI).

In a group of helminths obtained from the alimentary tract of a North American blue heron, *Ardea herodias* (P. Z. G. Lab., 1158), there were found twelve ascarides (Path. Hist., 1681; No. 34 of Synopsis, this journal), 8 females and 4 males. The host from which they were obtained died within a week after its reception in the Gardens, and unfortunately the precise records of the part of the alimentary tract inhabited by these worms were not made. There were also found fragments of a tapeworm (*T. unilateralis*, Dujardin) and a single example of an undescribed dispharagus; the autopsy protocol stating for the entire material that the parasites were found in the proventricle, stomach, and intestine. Presumably, inasmuch as the tapeworm fragments are much more likely to have been in the intestine and because the dispharagus was a solitary example, some of these ascarides were found in the upper portion of the tract.

The specimens are colorless, rigid, round in section, thickest posterior to middle of body length, tapering attenuately to the anterior and less finely posteriorly. Cuticle finely striated transversely, without alar expansions; longitudinal lateral lines well-marked.

The largest female measures 80 mm. in length, and at thickest level (about third fourth of length) 1.8 mm. in diameter. Head (Fig. 1) at base of lips 0.4 mm. in diameter; head rounded, with three prominent lips and well-marked

interlabia (Fig. 2). Lips nearly equal, the superior provided with two and each ventrolateral lip with one papilla. Superior lip (Fig. 3) four-sided, the angles rounded, anterior and lateral borders finely denticulate, lateral borders convex.

Lip deeply grooved; unpaired lobe of pulpa prominent; lateral lobes provided with anteromedian, anterior, and lateral lobules. Esophagus with triradiate lumen, slender, expanding posteriorly in clavate fashion, without bulb, but with a valve-like opening into the intestine. Intestine simple, straight, terminating at anus 1.1 mm. from tip of tail. Tail (Fig. 4) acutely conical. Vulva 30 mm. from head end. Ova (Fig. 5) taken from uterus measured 105 to 110 micromillimeters in length, 96 to 100 micromillimeters transversely, spheroidal in shape, with colorless shell marked by thickly set pits (giving at first impression the appearance of fine spines over the surface but really pitted, and the walls of the uterus where these ova lay having elevations corresponding with the pits); interior in advanced segmentation, brownish. The females in the posterior half of the body usually closely coiled.

The largest male measures 72 mm. in length and at thickest level (about the posterior third) 1.5 mm. in diameter. Anterior end as in female. Tail rigidly incurved, and at level of cloaca narrowed to 0.4 mm. in diameter, from which level it becomes bluntly rounded with a small acutely conical tip projecting 0.25 mm. beyond and curved dorsally, giving an ungulate appearance to the end of the tail (Figs. 6 and 7). Cloaca 0.15 mm. anterior to level of truncation. Genital spicules double, equal, curved, brownish, 1.3 mm. in length. Details of caudal papillæ determined with difficulty because of the rigid curving of the tail and the opacity of the specimens. On the small conical tip there are two pairs, No. 1 at posterior third of tip; No. 2 at anterior third of tip; No. 3 close to level of truncation, large and conical; No. 4 conical and smaller than No. 3, at level of cloaca; anterior to cloaca five or more pairs of smaller papillæ, more widely separated than Nos. 3 and 4.

Compared with *Ascaris serpentulus*, Rudolphi, these worms present many common features, and were at first regarded as probably identical. They differ however, very clearly in a number of characters. Among other points the absence of alar cuticular expansions at the anterior end, the more marked division or lobulation of the paired lobes of the pulp of the lips, the broader anterior margin of the lips, the smaller size and more spherical shape of the ova seem sufficient justification for regarding the worms in hand as of separate species. Differentiation from Linstow's *Ascaris reticulata* from *Ardea crocoi* (*Mitth. aus d. Zoöl. Samml. f. Naturk. in Berlin*, i, heft 2, p. 7) is readily made by the absence of interlabia and denticulation of the lips in the latter, as well as by other striking differences.

Oxyuris microtyphlon, n. s. (Plate VII).

Rudolphi (*Synopsis*, p. 285; No. 45) originally described under the name *Ascaris megatyphlon* certain small nematode parasites obtained from the cæca of two iguanas (*Iguana tuberculata*) preserved in alcohol, giving the specific name from the size of the intestine just back of the esophageal bulb. His general description is brief: "Hæ dimidiam ad tres lineas longæ, crassiusculæ, flaccidæ, quam plurimæ feminæ. *Caput* valvulis tribus acutiusculis. *Corpus* feminæ retrorsum incrassatum tandem longe subulatum; *maris* obtuso truncatum, *genitali* longo recto tenui in altero ante apicem exserto." His further discussion concerns the appearance of the esophagus and first part of the intestine, and his interpretation of its parts by analogy with the divisions of the alimentary canal of higher animals. Dujardin (*Hist. Nat. des Helminthes*, p. 146, Paris, 1845), identifying material from the same host with the above, erected a new genus, *Ozolaimus*, of which the worm in question formed for him the single species. His description follows: "Corps blanc fusiforme plus ou moins recourbé, long de 5 à 8 mm., 10 à 12 fois plus long que large; tête à deux lobes latéraux plus écartés vers le haut; bouche verticale; pharynx rétréci obtus, par les lobes internes, à travers lesquels on voit l'orifice triangulaire du canal œsophagien; œsophage brunâtre, long de 2.8 mm., traversé par un canal triangulaire, dont les arêtes sont occupées chacune par une petite gouttière tubuleuse; première partie de l'œsophage longue de 1.14 mm. large de 0.08 mm. au milieu, et renflée en un fuseau large de 0.16 mm. avant de se joindre par une sorte d'articulation avec le suivante; deuxième partie de l'œsophage longue de 1.66 mm., d'abord aussi large, puis retrécie jusqu'à n'avoir que 0.05 mm., et séparée, par un étranglement du ventricule large de 0.18 mm. turbiné; cavité interne du ventricule triangulaire, et revêtue par une membrane striée transversalement; intestin très-gonflé en arrière du ventricule, plus étroit en approchant de l'anus; tégument strié transversalement, et muni de deux bandes opposées granuleuses, larges de 0.05 mm.; stries écartées de 0.0045 mm. à 0.007 mm.

"*Mâle* long de 5 mm., large de 0.5 mm., recourbé en arrière; queue obliquement tronquée et comme ongiculée, ou terminée obliquement par un appendice déprimé, arqué; anus près de l'extrémité; spicule simple, presque droit, tres-aigu, long de 1.25 mm., large de 0.025 mm. pres de sa base, contenu dans une gaîne fibreuse et musculeuse qui le fait saillir en se contractant, retractile au moyen de deux muscles symétriques insérés à sa base.

"*Femelle* longue de 7.5 mm. à 8.2 mm., large de 0.66 mm. à 0.70 mm.; queue droite, amincie peu à peu et terminée en point mousse; anus situé a 0.25 mm. de l'extrémité; vulve saillante et boursoufflée, située au quart postérieur de la longeur, à 1.5 mm. de l'anus; uterus et oviductes repliés et

comme pelotonnes au-dessus de la vulve; œufs elliptiques longs de 0.096 mm. à 0.1 mm., larges de 0.053 mm."

Later, Schneider (*Monographie der Nematoden*, Berlin, 1866, p. 120) properly placed the worm in the genus *Oxyuris* and from poorly preserved material described the female as 3.5 mm. in length and the male 2.3 mm. "Mund mit (?) Lippen. Œsophagus mit einem Bulbus, darin ein Zahnapparat. Bursa wie ein Fingernagel gestaltet. Afterende kegelförmig weit nach hinten vorragend. Spiculum sehr lang. Papillen?" Schneider gives a plate of the tail of the male (Taf. VII, Fig. 9), which we have reproduced in outline (Fig. 9).

In 1905, Dr. C. Y. White, then pathologist to the Philadelphia Zoölogical Gardens, referred about 200 small nematodes, of which only 6 were males, which he had obtained at autopsy from the large intestine of an *Iguana tuberculata*, to the senior writer for identification. They followed closely the description of Dujardin, save that the ova were larger (118 x 53 to 133 x 68 microm.) and ellipsoidal rather than elliptical; there were three nearly equal lips to the mouth without apparent papillæ, and with the mouth-opening appearing triradiate between the lips instead of a vertical mouth with two lateral lobes. As in Dujardin's description, the anus was subterminal in the female, tail did not terminate finely, the vulva occupying the same relative position and presenting the same prominent appearance as described by this author. The tail of the male was unfortunately not studied in its details at the time, and the unused males were lost by a student to whom they were entrusted for histological study; but the general features of shape and size as well as the appearance and size of the spicule were noted. Lateral calcareous bands, as described by Dujardin, were constant in the specimens, and, too, scattered granules in the walls of the alimentary and genital tubes. Believing with Schneider that there is doubt as to the correctness of Dujardin's description of the mouth, we regard this material as identical with the oxyuris of the writers quoted.

Some months later (1906) Dr. Fox, the present pathologist to the Zoölogical Gardens, obtained at autopsy from the large intestine of another species of iguana (*Cyclura nubila*) numerous specimens of a smaller nematode, which on superficial examination was believed to be *Oxyuris megatyphlon*; but subsequent study has shown differences of structure constant and sufficient in character in our view to require reference of our specimens to a new but closely allied species, for which we propose the name *Oxyuris microtyphlon*. The notes of study, made October 30, 1906, follow: "Several hundred specimens of a small nematode worm obtained from the cecum of an iguana which had died in the Philadelphia Zoölogical Gardens (P. Z. G. Lab., 827) were submitted for identification, a very large proportion being quite small and undeveloped, the majority of the developed examples being non-gravid females. Of the developed specimens, the largest, females, measure 5 to 6 mm., or slightly more, in length, the males attaining a maximum length of 4.5 mm. The worms in transverse section are round; viewed in length are delicately fusiform, tapering anteriorly from the thickest part near the middle (0.3 to 0.5 mm.) to a rounded head which measures roughly between 0.05 and 0.1 mm. in diameter. Posteriorly the females (Figs. 5 and 6) taper gradually to the anus, where they measure about 0.2 mm. in thickness, the tail continuing about a millimeter beyond, straight and almost effilate, to a fine point. The tail of the male (Figs. 7 and 8) ends obliquely, closely resembling the tail of *Oxyuris megatyphlon* in general appearance, and presenting an ungulate tip as in the latter worm; the tail of male examples widely curved to ventral side. The worms are colorless, the cuticle transparent, delicate, and finely striated transversely. The longitudinal granular bands seen in *O. megatyphlon* are absent.

Mouth small, provided with three nearly equal lips (Fig. 3), each with two fairly prominent papillæ; esophagus (Figs. 5 and 7) long and straight, without the fusiform widening characteristic of *O. megatyphlon*, and showing a well-marked spheroidal ventricle (bulb) at the junction with the intestine proper. Compared with *O. megatyphlon* (Fig. 12) it presents a more slender esophagus; in fully developed females occupying from one-sixth to one-third the body length (being proportionately shorter and thicker in larger and gravid specimens, in which it seems crowded anteriorly), and in several males measured, nearly half of the full length. The esophageal bulb, like that of *O. megatyphlon*, contains a three-pieced armament; and in large females is about 0.2 mm. in diameter. The beginning of the intestine (the part called the cecum by Rudolphi) is generally smaller than in *O. megatyphlon*, but rather variable; the intestinal tube straight. In the female the anus is about a millimeter from the tip of the tail (from 0.8 to 1.4 mm. in different examples measured), and is guarded by two rather prominent transverse lips. Just within, upon the walls of the intestine, are several small rounded structures, probably anal glands. The anus of the male opens subterminally in a cloaca with the genital organs. Esophagus and intestine of both sexes brownish. The calcareous granules seen so numerously upon the walls of the intestine and generative tubes in *O. megatyphlon* are absent.

The generative apparatus (Fig. 5) of the female consists of two ovarian tubes and their oviducts, closely plicated along the intestine, which unite into a single uterine tube, this continuing as a thick-walled vagina to open at a vulvar orifice, guarded by two prominent transverse lips, a short distance (0.4 to 0.8 mm.) anterior to the anal orifice, the vulva being thus relatively more anterior than in *O. megatyphlon*. The fully formed ova (Fig. 1) are ellipsoid in shape, usually slightly flatter on one side than on the opposite, and range from 145 x 62 to 170 x 85 microm. in size (from measure-

ments of a dozen or more, obtained from several females). The shells are smooth, delicate, simple, somewhat pliant, and colorless; the vitelline substance yellow and granular; and with development a colorless, finely granular embryo takes its place. It is to be remarked further that the writer found several large females among the preserved material which contained well-formed larval worms in their interiors, these showing the general structural features of the adults. From one example as many as five of these larvæ were dragged in the dissection. It is not known whether these may not have developed within the parent from the ova after death of the worm (but this is suspected because developed ova and free larvæ were in no instance found together in any of the female worms) or whether the worm is ovoviviparous.

In the male the two tubular testes are disposed as the oviducts in the female, terminating in a sperm sac. The spicule (Figs. 4, 7 and 8) is single, long, and often double-curved, the distal curve directed dorsally (is sometimes straight). The cuticular tip of the tail (Fig. 4) of the male is straighter than that of *O. megatyphlon*, its sides infolded. It is supported ventrally by a median intracuticular spine which ends in four small prominences on the ventral side of the tip of the tail, and which shows in the median line of its base a second, smaller spine, bipartite at its free end. At the base of the latter, just back of the cloacal margin, there are on each side three small papillæ, the largest next the small median spine, the other two diminishing in size. The posterior lip of the cloaca is bilobed, the anterior trilobed, the median lobe the largest.

From the above description the general similarity to *O. megatyphlon* is apparent. The differences briefly stated in *resumé* are as follows: The adult worms are considerably smaller in size than *O. megatyphlon* (according to our measurements of *O. megatyphlon* and those of Dujardin; equal according to Rudolphi's, considerably larger according to Schneider's data); and the head is relatively smaller than in *O. megatyphlon* (our measurements). The papillary eminences on the lips are clear and constant; but these are not apparent in *O. megatyphlon*. The calcareous granules of the cuticular bands and in the walls of the alimentary and genital tubes are constant in *O. megatyphlon*, but are uniformly absent in the case of the present specimens. The fusiform swelling of the esophagus, regarded by Rudolphi as a proventricle, is constant in our specimens of *O. megatyphlon* (Fig. 12); is uniformly absent from *O. microtyphlon*. The size of the first part of the intestine (Rudolphi's cecum) is usually smaller than in *O. megatyphlon*. The vulva is relatively closer to the anus and considerably more anterior to the tip of the tail in the female of *O. microtyphlon* (cf. Figs. 5 and 11); and the tail is invariably long and finely drawn out instead of being slightly blunt as in *O. megatyphlon* (in the larval forms of the latter the tail is quite as in *O. microtyphlon*, and the larvæ are practically indistinguishable). The shape and general appearance of the ova are very similar, but the invariably larger size of those of the smaller worm (compare Figs. 1 and 2) is clear from the material examined by us (and they exceed by one-half to three-fourths the measurements given by Dujardin). Apparently (from camera lucida tracings) the ungulate tip of the tail of *O. megatyphlon* is slightly larger and is less straight than that of *O. microtyphlon*, but the failure to note the finer details of structure of the former prevents close comparison (compare Figs. 4 and 10). The difference from the tail of *O. megatyphlon* as depicted by Schneider (Fig. 9) is striking.

The iguana from which the examples in question were obtained was one purchased by the Zoölogical Gardens from an animal dealer, and no record as to its precise original habitat exists save that it was a Cuban iguana. It had been in the Gardens from June 29, 1906, until its death, September 11, 1906. The cause of death was not determined.

Globocephalus macaci, n. s. (Plate VIII).

In examining the intestine of a pig-tailed macaque, *Macacus nemestrinus* (P. Z. G. Lab., 508), there were found free in the lumen and in several tiny submucous cysts of the wall seven small nematodes (Path. Hist., 1673), which from their gross appearances were at first believed to be identical, but which upon careful examination proved to include five esophagostomes and two examples of a globocephalus. It is impossible at this time to indicate which of the specimens inhabited the cysts and which were free in the intestinal tube. Both specimens of the globocephalus were females and of nearly the same size. The larger measured 16 mm. in length, and at its thickest level, near the middle of the body length, 0.5 mm. in diameter. Cuticle delicate, transparent, distinctly striated transversely. The worm tapered regularly and gradually anteriorly to a rounded head measuring 0.25 mm. in transverse diameter; and posteriorly tapered to a finely conical, straight tail. No cuticular expansions or swellings. Head (Fig. 3) rounded and provided with a prominent spheroidal cavity, 0.17 mm. in transverse diameter, with an elliptical chitinous ring about the mouth and a triangular chitinous ring (sides convexly curved) at its base about the esophageal opening, these connected by a lateral longitudinal piece. Over the head the surface presents a peculiar mosaic appearance (Fig. 1) given by certain prism-like cells (feebly polarizing; are they crystalline?), whose ends underlie the cuticle about the buccal cavity. Mouth terminal, elliptical, its long axis dorsoventral, the chitinous ring about it measuring in long axis 0.14 mm., and in short axis 0.06 mm. Looking into the mouth, it seems to be surrounded by a row of fine spines, directed inwardly and toward the centre (the appearance may, however, be given by the bordering prism-like

cells). Within the mouth cavity (Figs. 2 and 3), springing from the base and apparently set in the chitinous ring about the esophageal opening, is an armature of three complexly curved chitinous plates. Esophagus 0.75 mm. long, flask-shaped, 0.25 mm. in diameter in its posterior and thicker part. At level of second third of esophagus, 0.65 mm. from front of head, on each side a pointed papilla projects above the cuticular surface (opening of cervical glands). No esophageal bulb. Intestine straight. Anus (Fig. 4, *a*) subterminal (0.14 mm. from tip of tail). Vulva (Fig. 4, *b*) prominent, provided with thick circular lip, 0.65 mm. anterior to tip of tail. Ova (Fig. 5) slightly yellowish, segmented, oval, with thin, colorless, unmarked wall, each with a slight thickening or tubercle at one pole; measure 0.064 to 0.07 mm. in length and 0.038 to 0.04 mm. in width.

Spiroptera incerta, n. s. (Plate IX).

Among all the types of verminous parasites derived from animals in the Zoological Gardens in the series studied by the writers by far the most numerous group has been made up of a small nematode obtained from the proventricles of a number of the inhabitants of the bird house, in which it would seem that a well-marked and strictly localized endemic has been for the past year or two, and is now, prevailing. The material studied (Path. Hist., 1109, 1120, 1453, 1463, 1613, 1616, 1618, 1619, 1620, 1621, 1622, 1623, 1624, 1625, 1626, 1627, 1628, 1629, 1630, 1631, 1644, 1661, 1672, 1675, 1686) includes examples obtained at autopsy from twenty-five birds, the parasites invariably occupying the proventricle and some times also being found in small numbers in the gizzard. The specimens, while often found free in the mass of mucus and food occupying the proventricle, were commonly found with the head end embedded in the more or less disintegrated lining membrane of the proventricle; the resulting mass often completely obstructing the tube and preventing the passage of food. The parasites varied much in the number found in each bird, the smallest number in the series being two in a valley quail, and the largest one hundred and thirty-four in a Rosehill parrakeet; commonly the grade of infestment was represented by twenty to forty worms; and generally the females outnumbered the males by about three or four or more to one. As a rule, in the case of infestment by larval or immature worms the number of parasites found ranged high, nearly a hundred or more than a hundred; from which it is suggested that ordinarily in the course of parasitism a number of the worms are dislodged from the proventricle, passed through the host's intestine and discharged. There is no evidence leading to the supposition that the adult parasites may locally produce the young forms; and in the few instances in which larval and partially developed or mature forms were encountered together the probability is that there took place repeated infestment. Six of the birds were infested by larval worms. One of these showed both larvæ and fully developed and gravid adults, the rest either larvæ alone or larvæ and immature adult forms. All of the latter birds were relatively recent admissions to the Gardens at time of death, having been in the collection from one or two to six or eight weeks. The one host having both gravid adult worms and larvæ had been in the collection over a year prior to its death; and, with the exception of three birds mentioned below as possibly introducing the parasites into the collection, the hosts were all inhabitants of the Gardens for several months to several years. From this it is suggested that the period required from the development from the egg to the mature adult stage is somewhere within six or eight weeks.

There is no positive information as to the time when first the parasites appeared in the collection; and their source is not clear. The first record (Path. Hist., 1109; August 28, 1906) concerned a Guatemalan amazon (P. Z. G. Lab., 790) and contains the statement that this was one of three birds showing the same parasites and same anatomical findings; that the three birds had been recently purchased for the collection, and that one died within two days after its reception; that they were placed in separate cages on their arrival, and that no other birds in the same portion of the house presented the same features of disease as these; that bunches of mucus containing the worms were found in the lower third of the distended esophagus in all three, acute enteritis in two, chronic enteritis in one, and parenchymatous degeneration of all the organs in all three. From this time forward the records of discovery have been numerous, including all twenty-five birds here referred to, as well as four or five more received since the present series was completed. The earlier examples and the greater number have been obtained from parrakeets and allied birds; but, evidently from unusual conditions prevailing in the bird house for the dissemination of the parasites, they have been found distributed in a variety of species, in several genera, and even in several families of hosts. The birds thus far found infested include the following; *Conurus pertinax*, two birds (P. Z. G. Lab., 1125, 1042); *Conurus leucotis*, one bird (P. Z. G. Lab., 1076); *Chrysotis guatemala*, one bird (P. Z. G. Lab., 790); *Chrysotis leucocephalus*, one bird (P. Z. G. Lab., 1131); *Chrysotis auripalliata*, one bird (P. Z. G. Lab., 910;) *Chrysotis ochroptera*, one bird (P. Z. G. Lab., 891); *Platycercus eximius*, five birds (P. Z. G. Lab., 843, 850, 862, 867, 889); *Platycercus barnardi*, one bird (P. Z. G. Lab., 1004); *Platycercus palladiceps*, two birds (P. Z. G. Lab., 876(?), 877); *Bolborhynchus monachus*, two birds (P. Z. G. Lab., 1049, 1164); *Bolborhynchus lineola*, one bird (P. Z. G. Lab., 871); *Palæornis fasciatus*, one bird (P. Z. G. Lab., 1052); *Protogerys virescens*, one bird (P. Z. G. Lab., 422); *Eclectus roratus*, one bird (P. Z. G. Lab., 1152); *Pæocephalus senegalus*, one

bird (P. Z. G. Lab., 823); and *Lophortyx californicus*, one bird (P. Z. G. Lab., 997). Recently, but not included in the present series, several of the pigeon family have also been found similarly infested.

From the very serious alterations found in the proventricle there can be no doubt of the serious importance of these parasites to the host, which unquestionably may by a serious grade of infestment be killed by the worms. In their earlier studies of the matter the writers searched, but in vain, for the presence of larvæ in the blood on the supposition that the parasites were true filariæ; but later determined the fact that the larva-laden ova are passed through the alimentary canal and are to be found in numbers in the fecal discharges. Search for an intermediate host has thus far been unavailing, the roaches, mice, and rats in the bird house having been repeatedly examined without success. Tentatively, therefore, the idea has been adopted that the ova with their enclosed larvæ, protected by the thick and firm walls of the eggs, are mechanically distributed, as by air currents, with dust from one cage to another, and in this manner get into the food or water of each bird and are swallowed therewith and develop from the egg within the mouth, esophagus, or proventricle of the new host. Based upon this view, it has been urged to the keepers of the collection that the cages are to be kept scrupulously clean, and, after the death of a bird or its transference, that the cages be sterilized. Apparently under such precautions there is some diminution of the occurrence of the parasites; but the interval has been too brief to permit certainty in this direction at the present time.

The structural characteristics of the worms are constant; but there is considerable variation in size of the mature specimens as obtained from different hosts, and often among the examples obtained from a single bird. The average maximum length of fully developed females was a little over 14 mm.; thickness, 0.45 mm.; average maximum length of males, 8 mm.; thickness, 0.34 mm. The smallest adults were occasionally but little more than half the size of the average; the largest female observed in the entire material was 20.5 mm. long and 0.6 mm. in diameter; the largest male observed, 12 mm. long and 0.35 mm. in diameter. The largest examples were found in the conures and in the Senegal parrot. The worms are of filarial shape (Fig. 1), long and slender, cylindrical in section, rigid and colorless. Thickest level of females at about two thirds of length from head; of males, near middle of body length. From these levels the specimens taper anteriorly in delicate manner to the head end, which at base of lips in a female of 12 mm. length measured 0.08 mm. in diameter (0.06 mm. in male somewhat over 8 mm. in length). Posteriorly the females taper uniformly and finely to an acutely conical straight tail (Fig. 6), with the tip slightly inclined dorsally; the tail of the male a little less acutely conical and curled ventrally. Cuticle finely striated transversely, transparent; and on each side at the head end the cuticle is raised into an uncertain and asymmetrical expansion (Fig. 2) with crenulated margin (in the female used for measurements reaching 1 mm. backward from head on one side and less than half this distance on the other). The head (Figs. 4 and 5) is small and is provided with six lips. Of these, two are large, thick lateral lips (Fig. 4, *a*), with broad and nearly straight anterior border, the sides incurved and the base about half the length of the anterior free border. These lips are armed with three prominent conical teeth on the anterior border; on their external surface, from base to anterior border, extends a depressed median line, on each side of which the lip substance rises in a rounded elevation. Midway between the free border and base on the external surface is a horizontal row of three small and easily overlooked papillæ. On either side of these lateral teeth is a smaller submedian lip (Fig. 4, *b* and *c*) with rounded margin and broad base, unarmed. Dorsally and ventrally between the two adjacent submedian lips is a sharp-edged prominence projecting into the oral cavity (Fig. 4, *e* and *f*) looking from the outside like an interlabial tooth. About the bases of the lips the body cuticle rises into a collar of small and irregular eminences. There is a well-marked oral cavity (Fig. 5, *f*), the base lying about the same distance back of the base of the lips as the lateral lips rise in height above their base; base of cavity horizontal, its lateral walls rising from it at nearly right angles. The esophagus (Figs. 1, 2, and 5, *g*) is long and slender (in male of over 8 mm. length it measures 2.5 mm. in length; in female of 12. mm. length, 3.5 mm.); for a short distance from the base of the oral cavity it is thin-walled and narrow, thereafter widening and becoming thicker-walled and definitely muscular. It opens into the intestine by a rather prominent valve-like arrangement. The intestine is straight and opens in the female subterminally (0.2 mm. from tip of tail); and in the male a little more anteriorly (0.35 mm. from tip of tail) in a cloaca. Caudal end of male (Fig. 8) provided with lateral alar cuticular expansions (not quite symmetrical) supported at base by irregular and small rays from the body wall,), enclosing a bursa. The cuticle within this bursa is arranged in long rectangular plates, running in the long axis of the worm and contrasting sharply with the transverse striæ of the rest of the cuticle. Within this bursa are ten pairs of papillæ and one unpaired precloacal papilla. These are arranged as follows from tip of tail forward: Nos. 1, 2, 3, and 4 (Figs. 8 and 9) are quite small and situated just in front of tip of tail, No. 2 (smaller than No. 3) and No. 3 nearly on same level (No. 2 median to No. 3); equal distances between Nos. 1, 3, and 4. No. 5 is about half-way between tip of tail and cloaca, larger than the above; No. 6 about half-way between No. 5 and cloaca, this pair not entirely symmetrical; No. 7 at or just in front of cloaca; Nos. 8, 9, and 10 in row anterior to No. 7, and separated

from No. 7 and each other successively by uniformly increasing distances. Nos. 5, 6, 7, 8, 9, and 10, and the unpaired precloacal papilla, considerably larger than Nos. 1, 2, 3, and 4. Male spicules unequal. Testicular tubes plicated along the intestine.

In the female there are two ovarian tubes, anterior and posterior, which with their oviducts lie densely folded along the intestine, nearly hiding the latter in the greater part of the length of the worm. These unite into a short and inconspicuous uterine and vaginal tube, which opens ventrally at an easily overlooked vulvar orifice (Fig. 1, *v*) within the first third of the length of the worm. Ova (Fig. 7) are colorless, elliptical in shape, with thick walls, each containing a more or less well-developed larval worm. They measure as an average 38 micromillimeters in length and 18 micromillimeters in transverse diameter (small examples as low as 34 x 16; largest examples as high as 42 x 20 micromillimeters).

The larval forms met were, as a rule, but 2 or 3 millimeters in length, and often showed some appearance as of undergoing moult, the old cuticle separating about the tail end of the worm. The mouth parts were less complex than in the adults. In the young sexual forms about the only feature of importance noted was the fact of the lack of development of the bursa by the formation of the lateral caudal expansions, the papillæ being, however, seen as in the older examples.

Spiroptera (?) *iguanæ*, n. s. (Plate X, Figs. 1 to 3).

From the lung of a Cuban iguana, *Cyclura nubila* (P. Z. G. Lab., 1127), a single specimen of a nematode worm (Path. Hist., 1641) was submitted for identification, in bad state of preservation, and for this reason mainly permitting only the following features to be determined. The worm, a male, measured 30 mm. in length and at its thickest level (near middle of length) 0.6 mm. in thickness. It was colorless, rigid, subcylindrical, nearly uniform in thickness for the greater part of its length, but anteriorly tapering to a rounded head end (which at 0.02 mm. back of the mouth measured 0.14 mm. in diameter), and posteriorly terminating in a bluntly conical, enrolled tail with rounded tip. Cuticle finely striated transversely; worm polymyarial. Mouth very small (0.02 mm. in diameter), the tissue about the head end rather badly broken, and the details of mouth structure uncertain. (Apparently there are three minute lips, four sided, with broad base, the anterior margin nearly straight and not as wide as base, the lateral margins convex; each lip with a single median prominence.) No buccal capsule. Esophagus long and slender, with triradiate lumen, without bulb, but widening posteriorly in delicate clavate manner before opening into intestine. Ventral surface of tail flattened to concave; uncertain from cuticular damage as to existence of cuticular expansions here and the formation thereby of a definite bursa. Tail tightly enrolled; tip of tail rounded, slightly constricted from the body of the tail, with several uncertain papilla-like prominences along its border as shown in drawing (Fig. 1). Cloaca 0.3 mm. from caudal end. Genital spicules (Fig. 2, *a* and *a*) unequal (0.27 and 0.55 mm.), grooved, the accessory piece relatively broad and flared out at distal end into a coarse barb. Eleven pairs of papillæ, of which six are precloacal; all closely set about the cloacal orifice, the most posterior being 0.21 and the most anterior 0.39 mm. from the tip of the tail.

The uncertainty of specific classification is seriously increased by the poor condition of the specimen and the fact that no female examples were obtained. The fact of the existence of six pairs of precloacal papillæ would render doubtful the propriety of regarding it among the filariæ or spiropteræ; but until further information is had the writers feel that the general features warrant a tentative retention among the spiropteræ, and would propose the specific name of *Spiroptera iguanæ*.

Dispharagus ardeæ, n. s. (Plate X, Figs. 4 to 6).

The following description is based upon a single female specimen (Path. Hist., 1681; No. 65, Synopsis, this journal) obtained from a North American blue heron, *Ardea herodias*, (P. Z. G. Lab., 1158), the same bird from which were also obtained the examples of ascarides above described under the name *Ascaris ardeæ*. The precise part of the alimentary tract from which the specimen was derived cannot be stated, inasmuch as the notes of autopsy merely mention the fact that the parasites, including the ascarides, fragments of a tapeworm (*T. unilateralis*, Duj.), and the present specimen, were "found in the proventricle, stomach, and intestine." Presumably the worm was a solitary example of its species in the host, being found alone and, although apparently fully developed, having no ova in its genital tubes. The specimen measures 17 mm. in length and 0.7 mm. in diameter at thickest level, near the middle of the body length; slightly attenuate anteriorly, tapering very much less posteriorly until close to the end of the tail, where it suddenly contracts into a conical tip bent strongly upon the dorsum. Specimen rigid, colorless; cuticle rather coarsely striated transversely. At the head end, beginning at the base of the prominent lateral lip on each side, there pass two raised sinuous lines, submedian, backward to nearly the middle of the body length, extending then dorsally and ventrally respectively to join similar lines upon the opposite side of the worm. The head at base of the lips measures 0.15 mm. in transverse diameter. Two lateral lips, each with double papillæ. Esophagus 2 mm. in length, made up of two portions, an anterior narrow portion 0.8 mm. long and 0.05 to 0.09 mm. in diameter, which suddenly enters a second wider portion 1.2 mm. long

and about 0.2 mm. in diameter. Intestine simple and straight. Anus 0.35 mm. from tip of tail. At level of anus the body suddenly narrows to form the conical end of the tail, presenting on each side of the anal orifice a marked ventrolateral rounded (mammillary) prominence. Vulva near middle of body length. Specimen non-gravid.

A BIOGRAPHICAL SKETCH OF JOHN REDMAN COXE, M.D., AND JOHN REDMAN, M.D.

[This biographical sketch was arranged by the late Miss Mary Clapier Coxe, a granddaughter of Dr. John Redmond Coxe. Portions of it were read before the Historical Club of the Medical Department of the University of Pennsylvania, at a meeting held several years ago, on the occasion of the presentation of an oil portrait of Dr. Coxe to the University of Pennsylvania. The sketch is published, with the exception of certain omissions, just as written by Miss Coxe.—Editors.]

JOHN REDMAN COXE, M.D.

Son of Daniel Coxe, of Trenton, and Sarah Redman. Born September 16, 1773, at Trenton. Married Sarah, daughter of Colonel John Cox, of Revolutionary fame. Died March 23, 1864, at Philadelphia, in his ninety-second year. Buried in Woodlands Cemetery.

Dr. Coxe was educated in Philadelphia, under the charge of his grandfather, Dr. John Redman. Went to school in London. Finished his classical education in Edinburgh, pursuing Botany and Natural History during the summer months. Attended hospitals.

1780. Returned to London. Attended Lectures on Anatomy and Chemistry.

1790. He returned to America, studying Medicine under Dr. Benjamin Rush for four years.

After receiving his diploma, he went to London, becoming for one year a house-pupil in the London Hospital. Went to Edinburgh and then to Paris, where he attended a course of lectures and was in the hospitals.

"In 1793, during the yellow fever visitation, he performed efficiently and with noteworthy energy and ability the duties of his office while with Dr. Rush." Dr. Coxe writes: "In 1794 there were but few drug-stores. Each M.D. had his

prescriptions prepared in his own office by students, which gave insight into practical pharmacy. Of this I had my full proportion while with Dr. Rush. I, some years afterward, opened a drug-store, which from its progressive extension occupied much time and broke in on my practical pursuits. At the death of Dr. Woodhouse, in 1809, I was elected to the Chair of Materia Medica; closed the drug business and in the duties of a professorship gradually relinquished a practice that had been lucrative."

1796. He returned to the United States and settled in Philadelphia, entering upon the practice of his profession.

1798. Filled the position of Port Physician. Was a physician of the Pennsylvania Hospital, and for five years Physician of the Philadelphia Dispensary.

1809. Was Professor of Chemistry in the University of Pennsylvania.

1818–1835. Was Professor of Materia Medica and Pharmacy in the University of Pennsylvania. Dr. John Redman Coxe may be considered as one of the first great medical writers in this country.

1794. Inaugural Essay on Inflammation.

1801. Pamphlet giving a short view of the importance and respectability of the science of Medicine. Observations on Combustion and Acidification, with a Theory of These Processes founded on the Phlogistic and Antiphlogistic Doctrines.

1802. Practical Observations on Vaccination or Inoculation for the Cow-Pock.

1804–1812. Medical Museum (eight volumes).

1806, '10, '14, '18, '30, '31. American Dispensatory.

1812. Emporium of Arts and Sciences (five volumes).

1827. Refutation of Harvey's claims to the discovery of the circulation of the blood.

1808–1817. Philadelphia Medical Dictionary.

1830. Observations on the Japan Plant.

1835. An appeal to the Medical Public from the Proceedings of the Trustees of the University of Pennsylvania vacating the Chair of Materia Medica and Pharmacy.

1845. Essays on Recognition of Friends in Another World, Phrenology in Connection with the Soul and as to the Existence of a Soul in Brutes.

1846. The Writings of Hippocrates and Galen Epitomized from the Original Latin Translations.

Dr. Coxe's writings on theological questions were very numerous. He spoke and read nine languages, Sanscrit being one of them.

He was a member of the Philosophical Society of Philadelphia, the Batavian Society of Sciences at Harlem, the Royal Medical Society of London, the Royal Society of Sciences of Copenhagen.

He filled the positions of Professor of Chemistry in the University of Pennsylvania, Professor of Materia Medica and Pharmacy in the same institution, Port Physician of Philadelphia, Physician of the Pennsylvania Hospital, Member of the Board of Trustees of the University of Pennsylvania. He was the founder of the association called the Philadelphia College of Pharmacy.

Dr. John Redman Coxe took great interest in both St. Andrew's and St. Luke's Episcopal Churches, having been one of the early founders and vestrymen in each: in St. Andrew's, when living at the corner of Ninth and Walnut Streets; in St. Luke's, when residing in the house he built, surrounded by a large garden, at Broad and Pine Streets. It was in this house that Dr. Coxe breathed his last breath, never having been sick in his life; never having had a headache; never going to the dentist. Without disease, he passed away at the advanced age of ninety-two.

In electrical phenomena, Dr. Coxe was among the first American scientists attracted to its study. His familiarity with the science of electricity led him to anticipate the alleged discoveries of Morse many years afterward. In a letter written to an English friend, published in Thomas Thompson's *Annals of Philosophy*, Dr. Coxe writes:

"I have contemplated this important agent (electricity) as a probable means of establishing telegraphic communications with as much rapidity as, and perhaps less expense than, any hitherto employed. I do not know how far experiment has determined galvanic action to be communicated by means of wires; but there is no reason to suppose it confined to limits, certainly not as to time. Now, by means of apparatus fixed at certain distances, as telegraph stations, by tubes for the decomposition of water and of metallic salts, etc., regularly ranged, such a key might be adopted as would be requisite to communicate words, sentences, figures, from one station to another; and soon to the end of the line. However fanciful and speculative, I have no doubt that, sooner or later, it will be rendered useful to practice." John Redman Coxe, M.D., Philadelphia, 1816. (See Silliman's *Principles of Physics*, p. 617.)

From the Historical Memoirs of the Philadelphia College of Pharmacy, published in 1869:

John Redman Coxe, M.D., was doubtless the leading spirit in the new movement of the Trustees, which, however, distasteful to the druggist and apothecaries, had a certain ground of reasonableness; and, as the event proved, had the happy effect of calling the attention of those not directly interested to the needs and requirements of the trade.

Dr. Coxe and his colleagues appear to have perceived what had been long before appreciated and acted upon in Europe, that the trade of the druggist and apothecary, involving peculiar responsibilities, and being inseparably connected with many delicate manipulations in connection with the vending and preparing of patent agents for the treatment

of disease, is one demanding scientific and practical education of a peculiar kind.

Resolutions of the Board of Trustees had already appeared in Poulson's *American Daily Advertiser:* "Resolved, that the degree of Master of Pharmacy be, and it is hereby instituted to be, conferred hereafter by the Trustees of the University."

1821. March 21, second meeting in Minute Book.

1822. This was the beginning of the College of Pharmacy, and the Act of Incorporation was read and accepted by the newly constituted body politic.

The first review of the *Journal of Pharmacy*, alluding to the Dispensatory, says:

"We cannot refrain from expressing our first conviction that, as a whole, this Dispensatory is the best in the English language on the subject of which it treats; and we know of no work so well calculated, in the eyes of our neighbors of Europe, to raise the character of American science."

"The American Dispensatory, comprehending the improvements in Dr. Duncan's Second Edition of the Edinburgh New Dispensatory, the arrangement simplified and adapted to the practice of Medicine and Pharmacy in the United States. By John Redman Coxe, M.D."

"An inquiry into the comparative effects of the Opium officianarum extracted from the Papaver somniferum, a White Poppy of Linnæus, and of that procured from the Lactuca Sativa, a common Cultivated Lettuce of America. Paper read before the American Philosophical Society, Nov. 24, 1797, by John Redman Coxe, M.D.," of which the opening sentences are the following:

"Gentlemen: In the boundless fields of inquiry which the book of nature opens to our view in the extensive regions of America, much remains to be investigated. Our forests, our fields, our rivers, mountains, and the bowels of the earth, alike invite attention from the philosophic mind. Too long has a supine inactivity prevented our benefiting by the bounty of nature. She is not coy, yet she requires pursuit from those who wish to secure her. Those alone who seek her will she meet with a smile, and conduct them to the temple of honor and fortune. Proteus-like, she assumes every form, and thus suits herself to the most fantastic imagination. The rugged aspect of the entrance to the various avenues of knowledge has deterred many from its pursuit, who, if they had made the least advance, would have perceived a speedy termination to the labyrinth before them, and a luxuriant prospect, unfolding to their view, growing more delightful as they proceed.

"Among the various objects which nature holds up to our view, none are more deserving of investigation than the vegetable kingdom. Here we discover plants fitted to nourish and preserve life, whilst others serve by their grateful fruits and odours to gratify the senses of taste and smell; or, by their brilliant colours, the eye of man.

"By the noble discovery of the art of dyeing many of these colours have become tributary to taste by their transmission to and fixation in other bodies. Nature is thus improved upon by rendering permanent and fixed these, her fugacious and transient moments.

"In Medecine, many of the most valuable articles of the Materia Medica are derived from this source; witness ipecacuanha, jalap, rhubarb, gamboge-bark, opium, etc. Wherever we look, we find Nature tributary to the labours of man. Her luxuriance is increased; she seems anxious to remunerate our fatigue, and to diminish, as far as is in her power, the curse inflicted upon the human race in the persons of our first parents of 'eating their bread with the sweat of the brow.'

"In the immense extent of the United States may be found every climate, from the torrid to the frigid zone. Let us not despair of ultimately possessing among ourselves all those invaluable sources of health and nutrition which are drawn from the vegetable kingdom in every part of the globe.

"The potato is a native of South America. Rhubarb, not natural to the climate of Great Britian, is cultivated. Opium, or Magnum Dei Donum, is an annual plant derived from the heads or capsules, from the milky juice in the capsules, and from the leaves and stalks of an annual plant found in Persia, Arabia, and other warm regions of Asia."

Preface to "An Appeal to the Medical Public from the Proceedings of the Trustees of the University of Pennsylvania, vacating the Chair of Materia Medica and Pharmacy:"

"I present the following statement to the public with extreme reluctance and pain. For nearly forty-five years I have been employed in the practice and study of Medicine, and in teaching it to others, in the city of Philadelphia; and at the close of this period myself and my family have been held up to derision for my alleged incompetency to discharge the duties of the Chair of Materia Medica, which I have had for more than fifteen years of that time.

"No one of common sensibility can be supposed to present to the public a statement which records such a result without extreme pain; but I have a duty, public and private, to perform, and I mean to perform it. I have suffered, and still do suffer, from unmerited persecution and contumely; from the gross and scandalous violence of young men, the pupils of the Medical School to whom its governors have seen fit to yield; and from the insidious artifices of older men, who have been willing to sacrifice me at the expense of the character of the University; but no sense of suffering shall deter me from exposing the injustice with which I have been treated. I executed all the duties of my station with what I supposed to be general approbation, until it was deemed expedient by some members of the Medical Faculty to supply my place with such as might better suit their views. I have at all times desired to sustain the Trustees of the University

in their lawful authority over the Medical Faculty, that they might appoint and control as they deemed best for the whole; and have never favored the system of Adjuncts, by which Professors named their successors, to the exclusion of all fair competitions by the Medical Professors generally, and of all real selection and choice by the Trustees; and, consequently, have taken no part in the cabals or intrigues that may have arisen on such occasions. I have never favored the plan of surrounding the University with medical institutes, whose posts should be filled by Professors of the University; that they might in this way sustain themselves even against the Trustees, if that should be necessary.

"I have taught in the Schools the doctrines which I deemed the wisest and best, without pausing to consider whether some other professor had not expressed himself in favor of different doctrines. I have ever opposed—and this is the head and front of my offending—some of the opinions taught by one of the most active of the professors, which I thought unsound; but in this I have followed the course of the Medical School when its reputation was at its height. I have done this, however, at all times respectfully, and not factiously.

"I have laboriously, faithfully, and to the disregard of all other interests, endeavored to do my duty, and my whole duty, in the Chair of Materia Medica, without giving either my morning or my evening hours to make favors with anyone; still less, to combine a party for my support or for the overthrow of anyone else. This course of proceeding has made me obnoxious to certain portions of the Medical Faculty which govern the rest; and has deprived me of the collateral support sufficient to resist the combined movement that has been made against me. The result is I am removed, without trial, without a hearing, without the common opportunity of defence. I relied on the justice of and firmness of the Trustees, and I have been disappointed.

"The Trustees themselves, as I conceive, have been the victims of the same injustice and intrigue by which I have been overthrown, and have had no power—or at least, thought they had none—to resist what some of them, I am certain, must have deemed an act of injustice to me and of great injury to the institution.

"The plan by which this has been brought about will be shown in the following pages.

"It began in an attempt by the other professors to degrade the science of Materia Medica itself; not succeeding in this, it assumed the form of an endeavor to enlarge the school by introducing a new Professor of the Institutes, without further expense to the pupils, but at the expense of the Chair of Materia Medica. This failing, it became necessary for the professors themselves to assail my competency, which also failed; as the members who made the charge were all of them unable to say that they had ever attended my lectures, and some of them were without the requisite capacity to decide the question, even had they attended.

"A regular assault upon my medical character was a difficult thing to manage, and it assumed various shapes. Sometimes it was said I taught too much or crowded my lectures with too much learning; sometimes, that I taught too little, or what everybody knew before. Even the pupils who had never read a medical book nor heard medical lectures were taught to uphold this language. Sometimes it was said I interfered with other professors by teaching what they had a right to teach; which, if my own inferiority was such as it was stated to be, could hardly have been a ground of very serious objection to the professor from whom it came. It was finally found that I was not likely to be broken down by any proceeding having regularity of form or purporting to rest on grounds that could be examined or, above all, put forward by responsible persons.

"Hence, a new system was adopted: The medical class was put into action. Young men of no experience, in some instances of no medical learning, of excited passions, and of ardent temper, were made the arbiters in a question concerning the learning of one of their teachers; and the Medical Faculty then appeared, but only appeared, to stand aloof. The plan was tried with too much gentleness at first, and it did not succeed; but at last, in consequence of various false suggestions—and among others the atrocious calumny that I had used or would use my power unworthily, to deprive students of their degrees—the requisite violence was prompted and employed. There was a secession of a large part of the class, accompanied by gross indecorums to the Professor; the other professors took no measures as a Faculty to restrain the class in the acts of violence and disorder; great efforts were made, as I understand, to abuse the public mind in regard to my capacity; and finally, the Trustees proceeded to quiet the rebellion by justifying it and sacrificing me.

"The public, particularly the medical public, will decide upon the justice of this sacrifice; and parents and guardians, the trustees and overseers of collegiate institutions, will ponder upon the tendency of such a precedent to promote the wholesome discipline of college and the education of youth.

"I arraign the Medical Faculty of the University for their connivance at this act of scandalous indecorum and resistance to collegiate authority; of this, at least, they have been guilty. The professors may say that they did not stimulate it, and such as choose may believe them; but they had (everyone knows that they had) the undoubted means to repress the disorder, and they would not use them. The charge of which they stand convicted is that they approved of the rebellion and violence, because, however disgraceful to the college, it served their turn. They approved it; and in conscience and common sense, it was their act, because

they would not repress it when they might. Theirs was the outrage, without the merit of openly assuming its responsibility; and some of them may have occasion to recollect the precedent hereafter."

(Signed) JOHN REDMAN COXE, M.D.

May 1, 1835.

SKETCHES OF EMINENT LIVING PHYSICIANS. John Redman Coxe, M.D., Late Professor of Materia Medica and Pharmacy in the University of Pennsylvania.

> "'With us there was a Doctor of Phisike.
> In all this world ne was there non him like,
> To speak of Phisike and Surgerie.
> Wel knew he the old Esculapius
> And Discorides and eke Rufus,
> Old Hippocras, Halli and Jallien,
> Seraphius, Damascene and Constantin,
> Bernard and Gaisden and Gilbertin.'

"Cato was standing in the Gallery of Natural Sciences in Philadelphia, admiring the hundreds of intelligent foreheads facing the venerable Chairman, Dr. Knight, of New Haven, the long hall, with gallery upon gallery, case upon case, and recess framework, was filled with the wonders of animate and inanimate nature, around him. There stood the king of birds, the ostrich, with several large eggs by him; here, the skeleton of the mastodon, the king of animals, presiding in quiet and solemn dignity over the large meeting. Around were lions, grinning over conquered serpents; horrid tigers and hyenas, almost in the act of howling; monkeys, from the great baboon to the most insignificant of the Simia. Great lithographs of the Samiens (schistose deposits, with the organic remains of these animals in them) lined the walls, surrounded by portraits of some of the most distinguished naturalists. Heaven itself threw a broad, but mellow light upon this immense collection.

"In the midst of the hum and subdued noise of this medical world, it was announced to the Chair and Meeting that a venerable disciple of Æsculapius was in the antechamber. On a motion being put and passed, a committee was appointed to wait upon him and invite him to take a seat in the American Medical Association.

"After a few minutes, the committee reappeared, escorting between them one who well represented the venerable appearance of the Father of Medicine, seventy-seven years of age. As if by magic, the whole assemblage rose and with uncovered heads, while the venerable patriarch passed through the throng up to the President's platform, and meekly stood by the officers of the meeting. His snowy locks hanging gracefully down, his head slightly bowed, the words of Dante appeared appropriate:

> "'I saw an old man standing by my side
> Alone, so worthy of reverence in his look
> That ne'er from son to father was more owed.'

"A few trembling words, thanking his medical sons (who had congregated from one end to the other of this vast republic) for their kindness, while a tear trickled down his furrowed cheek, and he sat down.

"Reader, that man was John Redman Coxe, M.D. The majority of those present had been his pupils and many of them seemed scarcely less aged than himself, a beautiful tribute to real learning.

"Dr. Coxe possesses one of the most valuable and largest private libraries in the United States, numbering, it is said, fifteen thousand volumes. Always a great antiquarian book-worm, he has for half a century been collecting, both in this country and in Europe, old and valuable books on Medicine, Theology, and other subjects. Cato thinks that Dr. Coxe could not better dispose of this immense library, particularly the medical portion of it, than to bequeath it, under proper regulations, as the foundation of a great medical library to be established in Philadelphia, where the medical profession, in making their pilgrimages to this, the Medical Mecca of America, might consult the best and most valued ancient and modern works on medicine and the collateral sciences. Coxe Medical Library, as the Harveyian or Hunterian Museum of England, would then be resorted to as are those great repositories of books and specimens. It is to be hoped that our venerable friend will thus bless, in parting with the world, the profession of his youth and mature manhood, and leave the world a memorial which will for all ages perpetuate his memory and elevate the medical profession in the New World. Harvey's foundation in London has, no doubt, had much to do with the perpetuation of his fame and the establishment of his claims as the discoverer of the circulation of the blood.

"Dr. Coxe it is supposed has never attended to a very extensive practice in Philadelphia, but has preferred attending to his pen and his duties as a public instructor. As the first introducer of the great Jennerian discovery, vaccination; as the inventor of an important remedy in croup and other infantile diseases, Coxe's Hive Syrup; as the Editor for many years of the Dispensatory; as a public teacher in one of the most practical branches of Medicine—he has swayed an immense influence over the medical profession of the United States.

"Never having enjoyed very robust physical health, always fully occupied with the learning of the profession, he has preferred to follow the more elevated and quiet occupation of writer and teacher."

His family influence was sufficient, in early life, to give him a place in the Board of Trustees of the University; his grandfather, Dr. John Redman, having long presided over the deliberations of that body. A student of the distinguished Dr. Benjamin Rush, he early found himself the successor of Dr. Woodhouse in the Chair of Chemistry in this school.

This Chair he filled for many years, and was succeeded by the well-known Dr. Robert Hare.

It is said that as a lecturer on chemistry he was more happy in explaining his experiments than in making them; and it is hinted that the paucity of apparatus and his lamentations over that which was broken or destroyed were occasioned by a disposition too penurious to afford the necessary outlay for the branch which he taught. This defect was amply compensated for by the liberality of his successor, whose apparatus demanded that a vessel should be chartered for its transfer to Washington, where it is now in the Smithsonian Institution.

It was, however, in the Chair of Materia Medica that Dr Coxe long flourished and declined. He suggested to the Trustees the propriety of establishing a course of lectures purely pharmaceutical, to which druggists and apothecaries should be admitted; and they acceded to the suggestion. Dr. Coxe thereafter lectured on Materia Medica and Pharmacy, until a sufficient number of druggists had been educated to form an association called the Philadelphia College of Pharmacy. This institution now is in a flourishing condition, and has already accomplished great good in elevating the character of the dispensing druggist and apothecary. Its journal is well known in Europe and America. Dr. Coxe may with justice be considered the founder of a more elevated Pharmacy in the United States. It is true that Medicine and Pharmacy have changed much since that time; this, however, does not detract from his influence upon the *then* condition of the profession.

"As a teacher of Materia Medica and Therapeutics, he was distinguished as a humoralist, and combated with the vigor of a giant the theories of his friend and colleague, Professor Chapman, which were out-and-out solidism. The old gentleman has now, in the evening of his days, seen the whole profession more ultra in humoralism than he had ever been, and the theories of his opponents swept away 'like the morning cloud and the early dawn.'"

His style of lecturing was an energetic conversational one, reading largely from notes, and continually combating some error of the past or of the present—particularly the latter. In this he was generally successful, on account of his vast erudition and superior knowledge. Whether from a reverence truly learned of the ancients, or from a disposition to cavil at all generally admitted facts, we know not, but Dr. Coxe preferred Galen to Hippocrates, considered Harvey as an impostor, and averred that the whole Materia Medica might with advantage be condensed into nine articles.

When Cato came on to the stage of action Dr. Coxe was not considered the popular professor of the school; but Cato always felt great partiality for the learning of Dr. Coxe, amusing himself by taking notes in Latin as the words fell from the old gentlemen's lips; and although he did not obtain from Professor Coxe a very accurate knowledge of the Materia Medica as taught in modern times, yet he considered himself fully compensated by the variety and amount of learning which could be obtained only through vast research over many volumes.

Early in this century Dr. Coxe projected and edited a journal called "The Medical Museum," which will always remain a monument of the industry and a point of reference for some of the best essays of the medical luminaries of that day.

"Personally, Dr. Coxe is about five feet six and a half inches high, with a good-sized head, covered with hair now snowy white, growing rather low over the forehead and brushed back; eyes black and piercing; a nose nearly of the Grecian contour; a good-sized mouth, made somewhat irregular by the projection of several front teeth; long arms; flat breast; thin in appearance. His dress, a black hat, rather broader brimmed than the fashion; a frock-coat, white cravat, black vest and pantaloons; a well-polished shoe, and a silver-headed cane. His light and active step might deceive one with an idea of his youth, had not time so blanched his hair, wrinkled his phiz, placed the annulus senilis upon his eyes, corrugated the skin, and enlarged the veins of his hands. His voice, never very strong, has almost the shrill pitch of a boy, especially when excited while lecturing."

> "A visage sterne and milde where both did growe
> Vice to contemne, in virtue to rejoice
> Amid great storms, whom grace assured so
> To live upright and smile at Fortune's choyce.
>
> "A hart where dreade was never so impasst
> To hide the thought that might the trouth anance,
> In neyther fortune loft, nor yet represt,
> To swell in welth or yield unto mischance."
>
> Cato.

Edward Jenner Coxe, M.D., University of Pa., 1823, son of John Redman Coxe, M.D., and Sarah, daughter of Colonel John Coxe, of Bloomsbury, Trenton, New Jersey, was born December 8, 1801, at Philadelphia. He married Mary Louisa, daughter of Louis Clapier, of Marseilles, France. He died at New Orleans, September 21, 1862. When twenty-three days old, he was vaccinated from the cow; so much faith had his father in the virus that he placed him in the arms of a man dying of smallpox. The disease did not prove contagious. The child was called Edward Jenner, after the great benefactor of mankind.

John Redman Coxe, M.D., was descended from a long line of medical and surgical ancestors, several of whom, at different periods, were physicians to the kings and queens of England.

1. The first Daniel Coxe, of Westminister, London, received, in 1648, the coat of arms granted by Parliament.

2. The second Daniel Coxe, son of the above-mentioned, was a gentleman of Stoke Newington, who died in 1686. His wife's name was Susannah.

Thomas Coxe, his nephew, was Physician in Ordinary to King Charles II., 1667.

3. The third Daniel Coxe, son of the foregoing, was born in London in 1648. He married Anne, daughter of Sir John Coldham, Lord Mayor of London, in 1696.

1669. Dr. Coxe's name appears on books of the University of Cambridge as M.D., "per literas regias."

1674. Elected as Member of the Royal Society.

1680. Admitted Honorary Fellow of the Royal College of Physicians in London.

He was the first to experiment on animals with the nicotine of tobacco. He published papers on Fixed Salts, extracting volatile salt and spirit out of vegetables.

He was Physician to Charles II, and Medical Attendant to Queen Anne.

Dr. Coxe is described as "a man of large wealth, gifted intellect, varied acquirements, and remarkable enterprise;" for on December 1, 1689, Dr. Coxe received a grant of the Province of Carolana in North America, by conveyance and letters patent passed. By William III in Council of that date. Carolana extended from Latitude 31 to 36 North, and from the Atlantic to the Pacific Ocean. Dr. Coxe was principal proprietor of the soil of New Jersey and sole proprietor of the government, he holding the office of Governor.

In 1700 he conceived the project of forming a commonwealth within the territory granted by Charles I to his attorney, Sir Robert Heath.

1699 (June 3). Was made a Member of the Society for the Propagation of the Gospel in Foreign Parts.

Dr. Daniel Coxe died January 19, 1730, aged ninety years. See description of the Province of Carolana, Smith's History of New Jersey, *Pennsylvania Historical Magazine*, vol. vii, 317.

4. The fourth Daniel, son of the foregoing Dr. Coxe, was born August 31, 1673, in London. He was the first of his name to come to America, which he did in 1701. He married Sarah Eckley, daughter of John Eckley, of Philadelphia. Died April 25, 1739. Buried in St. Mary's Church at Burlington, New Jersey.

This Daniel was a favorite of Lord Comburg, who appointed him Commander of the Forces in West Jersey; and afterward was known as Colonel Coxe. He was appointed one of the Associate Judges of the Supreme Court of the Province.

1722. Published a description of the English Province of Carolana.

1730. Received a Commission as Provincial Grand Master of the Free Masons for New York, New Jersey, and Pennsylvania, he being the first Masonic Grand Master in America. See Hough's Historical Sketch of Free Masonry in New Jersey.

5. The fifth Daniel Coxe, son of the foregoing Col. Coxe and Sarah Eckley, was born at Trenton in 1708. He married Abigail, daughter of Leonard Streate, Esq., of Middle Temple, Judge of Marshalsea Court.

Daniel Coxe died January 20, 1789.

In 1746 he was named as one of the Burgesses in the first charter of the Borough or Town of Trenton.

In 1747, owing to rioting, he was identified with the Proprietary Party in New York.

On an Estate of 132 acres, "Bellemont," twelve miles from Trenton, he led an uneventful life of prosperity. After his death the estate and slaves were sold. His will was dated January 25, 1750; proved January 21, 1758.

6. The sixth Daniel Coxe was the son of the foregoing. He was born in 1740, and married Sarah, daughter of John Redman, M.D., He died in London, in 1828.

1761. Studied law; was licensed as Attorney and Counsellor.

1792. Was licensed as a Sergeant.

He was a member of His Majesty's Council, upon which he was faithful and regular in attendance until the close of its existence in 1775. He was a zealous Tory. The burning of his handsome house, library, and pictures, at Trenton, by the British, who supposed him to be an American, during their pursuit of Washington in 1775, did not impair his attachment to the Royal Cause; as he went to New York, serving as President of an Association of Refugees, and remained there until the close of the war. See New Jersey Archives, vol. x, *Historical Magazine*, 1862.

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Grandfather of Dr. John Redman Coxe. Born in Philadelphia, February 27, 1722. Son of Joseph and Sarah Redman. Married Miss Mary Sobers, a lady of uncommon talents and accomplishments. Two sons died young; the oldest daughter, Ann, remained single; Sarah, the youngest, married Daniel Coxe, Esq., of Trenton, New Jersey, one of the King's Counsel.

Dr. John Redman died March 19, 1807, eighty-five years old, and was buried in the Presbyterian Church-yard on Arch Street above (?) Fifth.

He was educated with a view to his entrance into one of the liberal professions. After leaving the Academy he entered upon the study of Medicine with Dr. John Kearsley, one of the most respectable physicians of Philadelphia. At the expiration of his apprenticeship he went to Bermuda, where he practised several years with such success as to be able, with the property he inherited from his father and a small loan from a relative, to complete his studies in Europe. In Edinburgh he spent one year; another year in attending Guy's Hospital; and then attended lectures, dissections, and

hospitals in Paris. He graduated at the University of Leyden under Albinus, Zaubius, and Muschenbrock, at a time when that institution retained much of the reputation it had derived from the name of Boerhaave.

After receiving the highest honors of the profession, Dr. Redman returned to his native country and settled in Philadelphia. For a time he practised surgery and midwifery; but, owing to the delicacy of his health, he confined himself chiefly to the practice of Medicine.

His principles in Medicine were derived from the writings of Dr. Boerhaave, but his practice was formed by the rules

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of Dr. Sydenham. Dr. Redman considered a greater force of medicine necessary to cure Modern American than Modern British diseases; hence, he was a decided friend to depletion in all the violent diseases of our country. During the Yellow Fever of 1762 and 1793 he bled freely. In the diseases of old age he considered small and frequent bleedings as the first of remedies; and to them he was indebted for much of the ease he enjoyed in his descent down the hill of life.

In 1746, a MS., a course of public lectures on Anatomy at Edinburgh.

In 1759 he published a defence of Inoculation.

In 1762 he published a pamphlet on Yellow Fever, then prevalent.

A paper presented to the College of Physicians at the stated meeting September 7, 1793, was printed by order of the College in 1865, seventy-two years after its delivery.

He was elected one of the Physicians of the Pennsylvania Hospital soon after its establishment.

He became the first President of the College of Physicians; served as Trustee to the Colleges of Philadelphia and New Jersey; and more than once he refused to stand as a candidate for a seat in the Legislature of Pennsylvania before the American Revolution.

In 1784 he was elected an Elder of the Second Presbyterian Church. He was a stranger to bigotry, and often worshipped with sects of Christians differing in principle and forms with the Sect with which he was united.

He gave secretly and liberally to the poor; his old patients he visited two or three times a year. *Philadelphia Medical Museum*, vol. v., 1808; *Index to Medical and Philosophical Register*, p. 49, Library of the College of Physicians.

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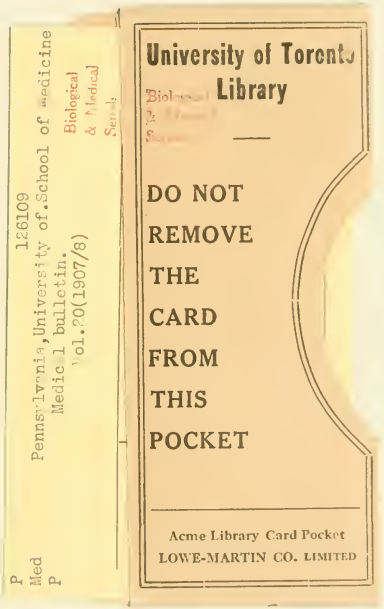
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